THE American Journal OF Gastroenterology

VOL. 21, NO. 1 JANUARY, 1954

SYMPOSIUM ON CIRRHOSIS OF THE LIVER

Correlation Between Needle Biopsy of the Liver and Infra-red Photography of the Abdomen in Cirrhosis of the Liver

Clinical Aspects of Cirrhosis: Observations on Hemorrhage and Hepatic Coma

Treatment of Cirrhosis of the Liver— Recent Innovations

Pathologic-Physiological Aspects of Cirrhosis of the Liver

Nineteenth Annual Convention
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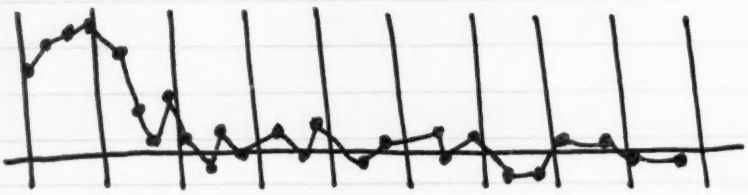

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1. Knight, V.: New York State J. Med. 50:2173 (Sept. 15) 1950.
2. Potterfield, T. G., and Starkweather, G. A.: J. Philadelphia Gen. Hosp. 2:6 (Jan.) 1951.
3. Swift, P. N.: Proc. Roy. Soc. Med. 44:1066 (Dec.) 1951.

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The American Journal of Gastroenterology

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

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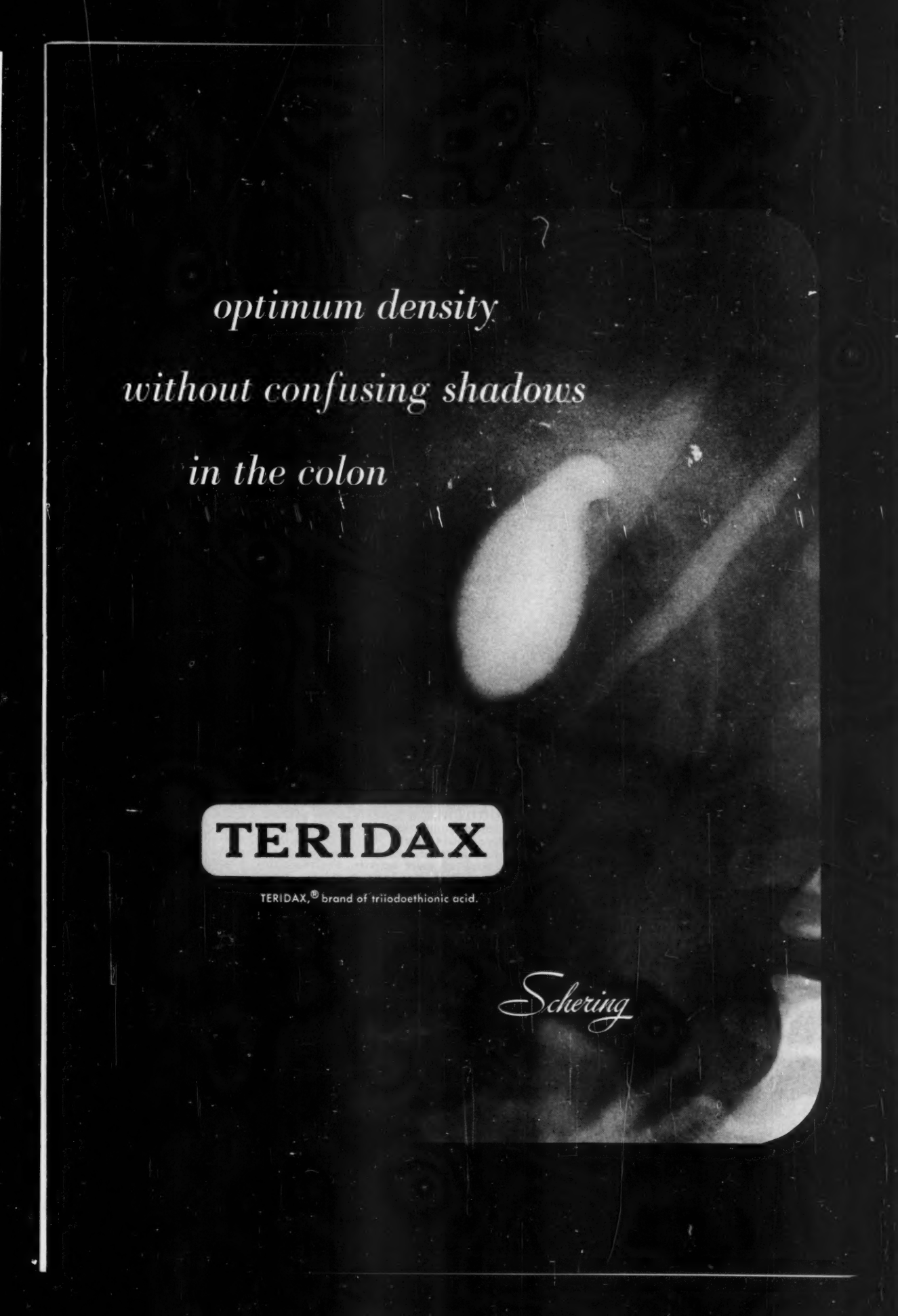
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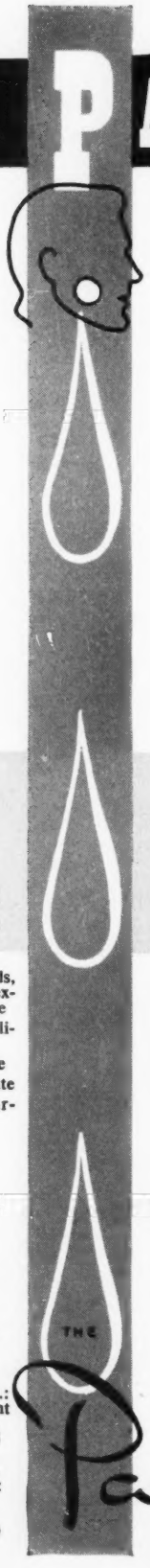

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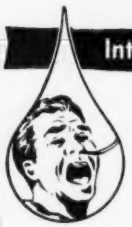

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Douthwaite, A. H.: Medical treatment of Peptic Ulcer, M. Press 227:195 (Feb. 27) 1952

Douthwaite, A. H. and Shaw, A. B.: The Control of Gastric Acidity, Brit. M. J. 2:180 (July 26) 1952

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SYMPOSIUM ON CIRRHOSIS OF THE LIVER

CORRELATION BETWEEN NEEDLE BIOPSY OF THE LIVER AND INFRA-RED PHOTOGRAPHY OF THE ABDOMEN IN CIRRHOSIS OF THE LIVER*†

I. R. JANKELSON, M.D.

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and

HENRY BAKER, M.D.

Boston, Mass.

Needle biopsy of the liver, is one of the newer methods of diagnosis of liver disease. Its safety is shown in the reported experiences of Gillman and Gillman[1], Schiff[2], Zamcheck[3], and others. Such safety is obtained only when the operator is properly trained and has had a wide experience. Certain important contraindications must be strictly considered, and preoperative hospital observation and treatment are necessary. A postoperative period of observation for at least 24 hours is likewise obligatory. In every case the bleeding, clotting, and prothrombin time must be normal, or nearly so. Unless these indices can be brought up to normal by preoperative treatment, a biopsy is contraindicated. The patient must be cooperative. It should not be done on ambulatory, uncooperative, or extremely ill patients. The operator should be prepared to transfuse the patient if there should be evidence of internal bleeding.

A definite diagnosis based on histologic evidence of a biopsy can be made in more than 90 per cent of cases in diffuse liver disease, as in liver cirrhosis and in a somewhat lower percentage in disease characterized by focal involvement.

The procedure is neither safe, nor diagnostic when performed by inexperienced operators, since under such circumstances, many specimens are unsatis-

*Read before the Eighteenth Annual Convention of the National Gastroenterological Association, Los Angeles, Calif., 12, 13, 14 October 1953.

†From 1st and 3rd (Tufts) Medical Services of Boston City Hospital and Mallory Institute of Pathology.

Aided by a grant from the James Striar Family Foundation.

factory for a histologic diagnosis. Except for experimental purposes, a needle biopsy of the liver is not indicated unless a proper diagnosis cannot be made by other, simpler methods, including batteries of liver function tests, repeated at short intervals. There is, however, a very considerable group of patients with liver disease with or without jaundice in whom a definitive diagnosis is not possible even after prolonged observation and intensive clinical studies.

In 1938, Jankelson and Baker[4] reported their experiences with infra-red photography of the abdominal wall and established a definite pattern of collateral circulation in cirrhosis of the liver. The finer arborations of the superficial

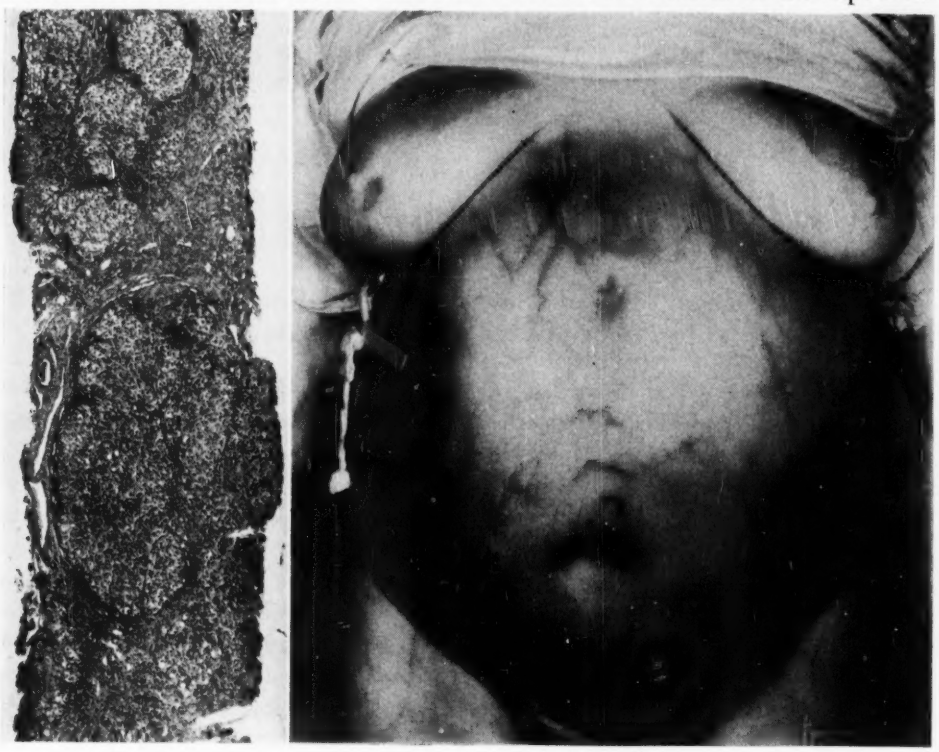

Fig. 1a Fig. 1b

Fig. 1a—The biopsy shows moderately advanced fibrosis of the liver. There are abundant regenerated nodules of liver tissue, some of which show small amounts of fat.

Fig. 1b—There is definite evidence of an abdominal venous pattern as shown by infra-red photography. These veins are scattered throughout the abdominal wall. There is relatively little anastomoses between these veins.

veins of the abdominal wall, which are diagnostic of portal hypertension, can neither be seen by the naked eye, nor demonstrated on ordinary photographic films. Larger, longitudinal, venous channels may be seen in a variety of conditions including malnutrition, pregnancy, abdominal tumors and nonhepatic ascites. A method of visualizing the superficial abdominal veins with the aid of x-ray goggles was described. In our experience this method is not satisfactory.

The development of widespread anastomoses of the veins of the abdominal wall depend on at least two factors: the portal hypertension, and its duration. Hence, in acute portal thrombosis or pyelophlebitis it is not demonstrable. The presence of such venous arborations is, then, for all practical purposes limited to cirrhosis of the liver and Banti's syndrome with long-standing portal or splenic hypertension.

This study is done in an attempt to correlate the histologic evidence of cirrhosis of the liver obtained by aspiration liver biopsy and the photographic

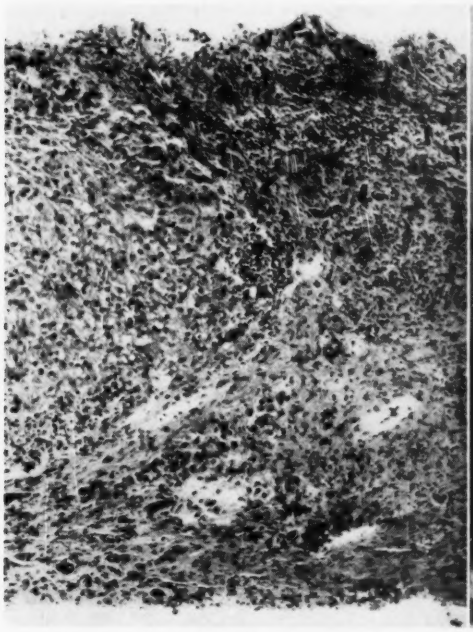

Fig. 2a

Fig. 2b

Fig. 2a—The biopsy specimen shows marked fibrosis of the portal areas with encroachment upon the neighboring liver cells by immature fibroblasts. There are many small nodules of regeneration. In addition there is evidence of cellular degeneration of liver cells with some necrosis. Around some of the degenerating liver cells definite polymorphonuclear infiltration can be seen.

Fig. 2b—The infra-red photograph shows numerous large longitudinal superficial veins with many anastomoses between them. The entire abdominal wall is involved, more marked in its upper half.

method of demonstrating the newly formed anastomoses of superficial veins of the abdominal wall.

Clinical Observations

A few typical cases are demonstrated representing a large group of cases examined during the last five years, during which time needle biopsy of the liver was employed in this hospital. Infra-red photographs were made of the

abdominal wall of a group of patients with a great variety of diseases not involving the liver as control cases. None of these showed the venous pattern which will be shown presently. Likewise, patients with other liver disease, such as acute infectious hepatitis, carcinoma of the liver, and fatty liver persistently showed negative infra-red photographs.

We are presenting photomicrographs of the liver, and infra-red photographs of a selected group of patients with anatomically proven cirrhosis of the liver, and a few of the control group. Time will not permit a clinical analysis of these cases. A complete study of the material will be presented elsewhere.

Case 1:—This is a 49 year old, white, separated waitress who is a chronic alcoholic and has had multiple hospital admissions for cirrhosis of the liver with many complications, including jaundice, ascites, and hematemesis. The patient

Fig. 3a Fig. 3b Fig. 3c

Fig. 3a—The photomicrograph shows that the liver is the seat of a diffuse fibrotic process in which bands of fibrous tissue extend in all directions from the portal triads. There is little evidence of inflammation or degeneration.

Fig. 3b—This infra-red photograph shows marked enlargement of the abdominal veins, showing a longitudinal distribution with many transverse anastomoses between them. Note the scar of the previous operation.

Fig. 3c—For comparison an ordinary photograph of the abdomen is also shown.

expired in hepatic coma six months after the needle biopsy and infra-red photography.

Diagnosis:—Moderately severe alcoholic cirrhosis.

Case 2:—A 44 year old, single bartender was admitted to the hospital because of bilateral ankle swelling of 4 days duration. He is strongly alcoholic and shows icteric sclerae and marked ascites with a palpable liver 5 fingers below the costal margin.

Diagnosis:—Active alcoholic cirrhosis (marked).

Case 3:—A 58 year old, white female, a chronic wine drinker, was admitted for the fifth time for persistent liver disease. In the past she had jaundice and

ascites. She was operated on for an incarcerated inguinal hernia 2 months before this admission. There is marked ascites, but no jaundice.

Diagnosis:—Cirrhosis of the liver, type undetermined.

Case 4:—A 50 year old, chronic alcoholic who was quite well until two months prior to admission developed swelling of his legs, unsteady gait, and diplopia. He was admitted to the hospital where he had slight icterus. There were many typical spiders over the chest and shoulders. Ankle edema was present. An umbilical hernia was observed. There was no ascites, and the liver

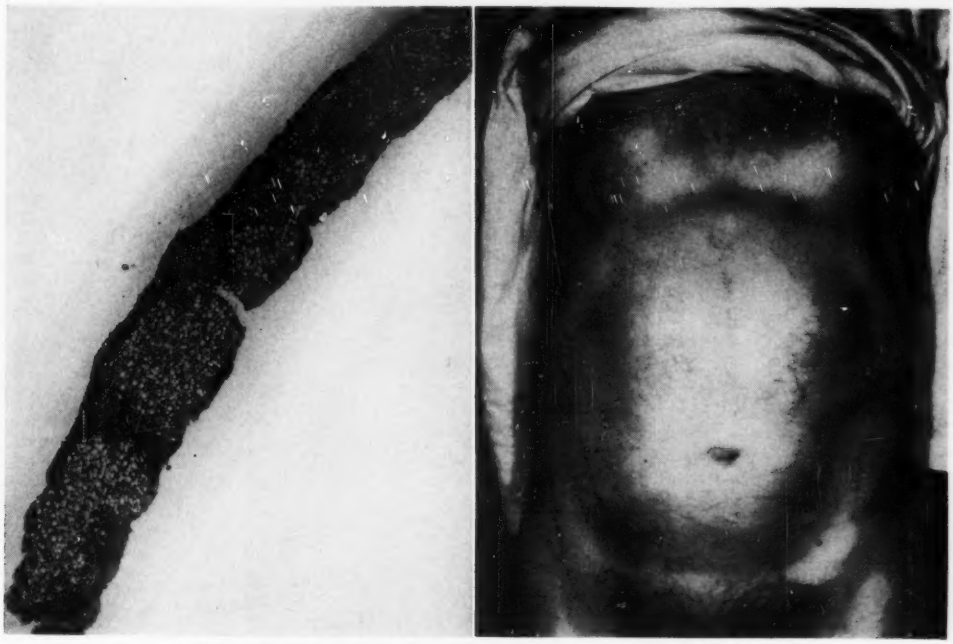

Fig. 4a Fig. 4b

Fig. 4a—This photomicrograph shows the liver parenchyma to be almost completely replaced by large fat vacuoles. The portal areas show a slight but definite increase in fibrous connective tissue as well as a small number of round cells. There is no evidence of diffuse inflammation or marked fibrosis. An occasional bile canaliculus is distended with green staining bile.

Fig. 4b—There are a few demonstrable veins in both flanks and upper half of the abdomen on the infra-red photograph. There are, however, no anastomoses between these veins.

edge was percussed 7 finger breadths below the right costal margin. Spleen was not felt.

Patient responded to a nutritious diet, losing his jaundice, ankle edema, and the liver function tests improved.

Diagnosis:—Fatty liver and early cirrhosis; Wernicke's Syndrome; polyneuropathy.

Case 5:—A 65 year old salesman was admitted to the hospital for intestinal obstruction. At operation a large cancer involving the cecum and ascending colon was found. He had widespread metastases to the regional nodes and liver. Resection of the lesion was impossible. An ileostomy was performed to relieve the obstruction.

Diagnosis:—Cancer of the colon with liver metastases.

Case 6:—A 36 year old female was admitted to the hospital because of painless jaundice of 10 days' duration.

Fig. 5

Fig. 5—Shows the ileostomy opening and a large ventral hernia. On the infra-red photograph longitudinal superficial veins of the abdomen are shown. There are no anastomoses between them.

Diagnosis:—Acute infectious hepatitis.

Case 7:—Enlargement of spleen of undetermined origin without histologic evidence of liver disease.

Discussion

The few cases shown here are representative of a much larger number studied. There is good correlation between the evidence obtained through an aspiration biopsy and infra-red photography in proven instances of cirrhosis

of the liver. The liver biopsy permits of histologic study of living tissue. In cirrhosis of the liver it determines the degree of fibrosis, destruction and regeneration of liver cells, infiltration with fat, plasma cells, leucocytes or lymphocytes. The infra-red photographic evidence indicates long-standing portal hypertension, more or less paralleling the amount of fibrous tissue within the liver. Cirrhosis, of short, clinical duration, shows relatively little or no anastomotic veins.

A liver biopsy permits also the diagnosis of other liver diseases including biliary obstruction and, with some reservations, the absence of liver disease. The

Fig. 6a

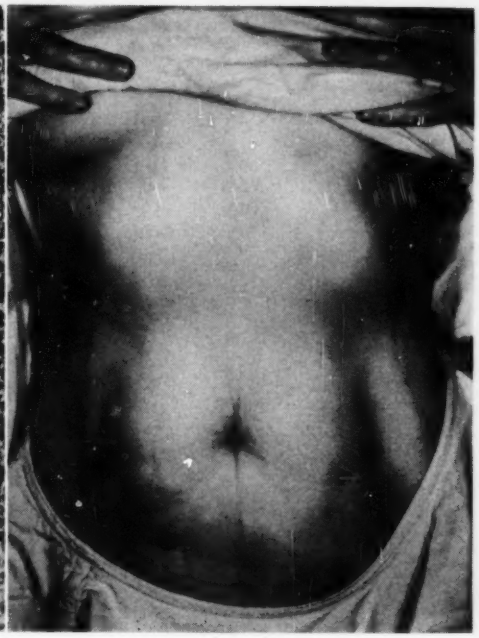

Fig. 6b

Fig. 6a—The photomicrograph of the aspiration biopsy shows the following: There are distended bile canaliculi filled with green staining bile. The sinusoids are infiltrated with cells. There is cellular disarray and some areas of cellular necrosis. There is intense infiltration of the pericholangiolar tissue with round cells. No inflammatory cells or bile seen in the larger bile ducts.

Fig. 6b—Infra-red photography shows no demonstrable veins of the abdomen.

photographic method is non-contributory except in cirrhosis of the liver. On the one hand liver biopsy requires hospitalization of the patient for 1 to 2 days, carries a calculated risk of hemorrhage and bile peritonitis and is at times painful. Not infrequently, in cases where a needle liver biopsy is indicated, conditions exist which make this procedure inadvisable or hazardous. Infra-red photography on the other hand is not dangerous, is neither painful nor objectionable to the patient, and can be performed on ambulatory as well as hospitalized patients. Needle biopsy of the liver should be done by properly trained or carefully

supervised operators, who may not be available in many hospitals, particularly in community and nonteaching institutions. Infra-red photography does not require special skill or experience, and the interpretation of the photographs is simple. The two methods are complementary in the diagnosis of cirrhosis of the liver. It is not fully appreciated that, by repeated liver aspirations, the progress of the disease can be followed. Thus, liver biopsy can contribute to the prognosis and proper evaluation of treatment in liver disease. Since infra-red photographic evidence depends on the formation of new anastomoses between the veins of the abdominal wall, this method gives no information as to regression of the

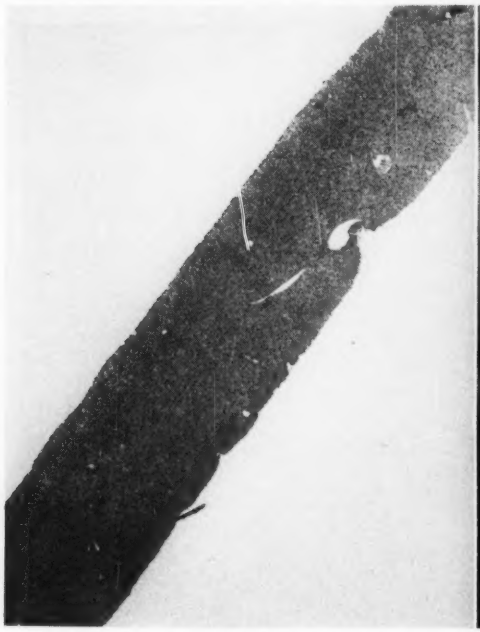

Fig. 7a

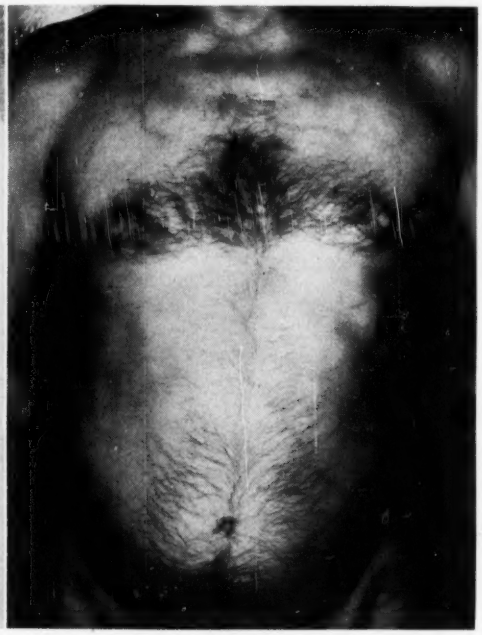

Fig. 7b

Fig. 7a—Photomicrograph of liver biopsy shows normal architecture of the liver without abnormal cells, fatty or fibrous infiltration. The cells are regular; the nuclei well visualized. The canaliculi are not dilated and do not contan bile. The portal triads are normal.

Fig. 7b—The corresponding infra-red photograph shows no visible superficial veins. The spleen is outlined on the skin by a pencil.

disease. Progression of the disease may be accompanied by more arborations of the veins which, once formed, do not disappear even if portal hypertension is relieved.

Nevertheless, the simplicity and safety of the photographic method recommends it as a valuable procedure in the diagnosis of cirrhosis of the liver. It does not replace needle biopsy of the liver in the diagnosis of liver disease in general and of cirrhosis in particular. Both methods, judiciously and selectively applied aid in the diagnosis of cirrhosis of the liver.

Summary

The correlation between aspiration liver biopsy and infra-red photography of the abdominal wall in cirrhosis of the liver is demonstrated in a selected group of cases. Liver biopsy not only permits of a histologic diagnosis of cirrhosis, but where repeated, helps in evaluating the management of a patient. These latter data cannot be obtained by infra-red photography. The two methods are complementary in the diagnosis of cirrhosis of the liver. Needle biopsy of the liver as a diagnostic procedure can be utilized in confirming the presence of other diseases of the liver and to demonstrate absence of liver involvement. The infra-red photographic method, however, is limited in its scope to demonstration of long-standing portal hypertension.

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CLINICAL ASPECTS OF CIRRHOSIS: OBSERVATIONS ON HEMORRHAGE AND HEPATIC COMA*

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and

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Although the gross pathology of cirrhosis of the liver had been recognized for many years, Laennec gave the first adequate description of the disease in 1819, and provided us with its name, derived from the greek word "Kirrhos" meaning orange colored. An accurate clinical description of cirrhosis, which could stand today, was made by Shattuck, the Professor of Medicine at Harvard, at a clinic for medical students in 1888[1]. The discussion of a case presented sixty-five years ago is interesting because the description of the clinical picture of the disease made by an authority at that time compares favorably to our present day understanding of it.

In the succeeding sixty-five years we have come to understand more of the pathological physiology of cirrhosis from use of modern bio-chemical methods and animal experimentation. The punch biopsy has provided better understanding of the pathological stages and thus prognosis, but liver function tests have added disappointingly little to our ability to correctly diagnose types of liver disease. The exact role which alcohol plays in the etiology of cirrhosis is not much better understood than it was in Shattuck's day, although we have learned that malnutrition is tremendously important and suspect that alcohol has its evil effects indirectly, by substituting calories from protein with calories from alcohol. Additional important clinical features of cirrhosis learned in recent years include the effects of portal hypertension and the significance of esophageal varices. Also we are beginning to learn something about the pathologic physiology of hepatic coma.

The authors have analyzed 162 cases of cirrhosis treated at Wadsworth V. A. Hospital from the point of view of cause of death, of hepatic coma, and of hemorrhage. This paper is concerned with a discussion of these clinical aspects of the disease.

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Case Material

The material comprises two groups of cases. The first group consisted of the cases of cirrhosis found among 625 consecutive autopsies in 1949. In this autopsy series the causes of death were analyzed (Table I).

The second group was derived from an analysis of 118 clinical records selected at random from all the patients discharged with a diagnosis of cirrhosis in 1951 and 1952. The diagnosis was established by clearcut history, physical, and laboratory findings, and confirmed, in the majority, by needle biopsy. In this

TABLE I

Analysis of 625 Consecutive Autopsies Performed From January 1, 1949–December 31, 1949

	Number	Per Cent
Autopsies in which cirrhosis was present	44	7
Of these:		
Cirrhosis caused death in	20	3.2
Cirrhosis contributed to death in	8	1.3
Cirrhosis unrelated to death in	16	2.5
Cause of death in 44 patients with cirrhosis		
Hemorrhage from varices	5	
Hepatic coma caused by hemorrhage	7	
Hepatic coma, alone	8	
Hepatoma	1	
Bleeding gastric ulcer	1	
Perforated duodenal ulcer	1	
Pneumonia	5	
Pulmonary tuberculosis	2	
Meningitis	1	
Cardiovascular disease	5	
Cerebral hemorrhage	1	
Subdural hematoma	1	
Postoperative	3	
Carcinoma	2	
Suicide	1	
Peptic Ulcer–Occurred in 7 patients of the 44 with cirrhosis		15.2
Occurred in 64 patients of 581 without cirrhosis		11.0
Hepatoma (primary) occurred in 2 of 44 cirrhotics and occurred in none of 581 noncirrhotics		4.5

clinical series the patients who had hepatic coma, gastrointestinal hemorrhage, or both, were analyzed, as well as the causes of death (Table II).

Etiological aspects in this study were not considered since the exact etiology is frequently difficult or impossible to establish. Suffice it to say that the vast majority of both groups had a history of alcoholism with inadequate diet, and were examples of classical Lannec's cirrhosis.

Causes of Death

In the 625 cases comprising the autopsy series 44 or 7.0 per cent had cirrhosis. In 28 or 63.6 per cent of these 44 cases, cirrhosis was either the cause

of death or an important contributory cause. The remaining 16 cases (36.4 per cent) either were not suspected of having cirrhosis during life or had no clinical disability resulting from the disease and died of unrelated causes. This reflects a high incidence of compensated cirrhosis, demonstrating that the disease may exist for considerable periods of time without symptoms.

In the 118 patients comprising the clinical series, all of whom had signs of cirrhosis, 58 died, and 44 of these 58 patients, or 76 per cent, died of cirrhosis. The other 24 per cent died of apparently unrelated causes although cirrhosis doubtless contributed to death in some of these. Forty-two of the 44 who died of cirrhosis had hemorrhage from esophageal varices, hepatic coma, or both. One patient had hepatorenal syndrome and another died of hemorrhage from diaphragmatic varices.

TABLE II

CAUSE OF DEATH IN 58 PATIENTS WITH CLINICAL DIAGNOSIS OF CIRRHOSIS*

	Number	Per Cent
Hemorrhage from varices	14	24.2
Hepatic coma caused by gastrointestinal hemorrhage	13	22.4
Hepatic coma, alone	15	25.9
Bleeding diaphragmatic varices with hemoperitoneum	1	1.7
Hepatorenal syndrome	1	1.7
Bleeding peptic ulcer	3	5.3
Perforated peptic ulcer	1	1.7
Pneumonia	2	3.4
Meningitis	1	1.7
Miliary tbc	1	1.7
Cardiovascular disease	4	6.9
Carcinoma lung	1	1.7
Cause unknown	1	1.7
	58	100.0

*Of 118 patients with clinical diagnosis of cirrhosis, 58 died and 60 recovered sufficiently to be discharged from the hospital.

In both series, either hemorrhage or liver failure accounted for over 90 per cent of the deaths in which cirrhosis was the direct cause of death. Hemorrhage resulting from portal hypertension accounted for death, apparently from blood loss and exsanguination, in 14 of the clinical series, and in five of the autopsy series. In other patients a severe hemorrhage which was controlled had occurred. These patients then went on to develop hepatic coma secondary to the additional liver damage occasioned by shock and anoxemia at the time of the hemorrhage. There were 13 deaths from hepatic coma secondary to recent hemorrhage in the clinical series and seven in the autopsy series. Finally hepatic coma alone, not precipitated by hemorrhage, was the cause of death in 15 of the clinical series and eight of the autopsy series.

HEPATIC COMA

It has been known since earliest times that the appearance of symptoms referable to the central nervous system in patients with disease of the liver is

a grave prognostic sign. Patients who die of liver disease often present, terminally, some of these central nervous system signs which then progress into coma. Death nearly always ensues when the coma stage is reached, though recovery may occur. The neurological signs and symptoms of hepatic coma have been well described by Adams and Foley[2]. The patient with advanced liver disease, regardless of the cause becomes suddenly drowsy, speaks with slurred speech, and becomes disoriented. He may become noisy and confused, sometimes utters piercing cries (especially children with liver necrosis), but is more likely to be quiet, appearing to lapse into deep sleep, from which he cannot be aroused. Convulsions are comparatively rare. Before the comatose stage is reached a characteristic tremor has been described, known as the "flapping tremor". This is absent at rest but appears if the patient holds his arms forward with hands and fingers extended. The tremor is then seen as an irregular, coarse flexion-extension movement of the wrist or metacarpophalangeal joints. Various other neurological signs may be seen such as spastic reflexes, rigidity of extremities or cranial nerve palsies.

Foley, Watson and Adams[3] described electroencephalographic changes which are seen in hepatic coma, in 1950. They obtained tracings in 26 patients with severe liver disease, of whom 16 were in coma, and correlated the EEG with neurological and clinical evaluation. They found a definite and distinct pattern in the coma group consisting of bursts of slow waves of two-per-second frequency alternating with intervals of normal activity. Although slowing may occur in disturbance of consciousness from any cause, the alternation between slow waves and normal activity was only found in hepatic coma. They felt that the explanation for hepatic coma as evidenced by the EEG abnormalities might be a metabolic disturbance acting on the thalamo-cortical systems.

The explanation for hepatic coma on a biochemical basis is not at hand. It has been found that liver function tests and histologic findings are no different in hepatic coma from what is found in severe liver disease without coma. In general this is also true of biochemical alterations which may occur, such as electrolyte abnormalities, elevation of blood pyruvate, amino acid changes, etc.

The relationship of the ammonium ion to the neurological disturbances of liver failure have been recently emphasized[4,5] although reports in the German, Scandinavian and French literature[6,7,8] had indicated as early as 1927 that elevated blood ammonia levels occurred in hepatic coma, and that patients with cirrhosis did not tolerate certain nitrogenous substances. Studying the effect of cation-exchange resins in the treatment of ascites and edema associated with liver disease, Gabuzda, Phillips and Davidson[4] noticed that six out of eight patients receiving ammonium-containing resins developed neurologic manifestations resembling those of impending hepatic coma. Phillips, Schwartz, Gabuzda and Davidson[5] studied further the effect of the ammonia radical on neurologic manifestations. They were able to produce mental symptoms, EEG changes, and at times the typical flapping tremor, by administering ammonium potassium

cation-exchange resin, ammonium chloride, ammonium citrate, urea, and a high protein intake to patients with cirrhosis. When each of these agents were withdrawn the signs and symptoms disappeared.

A further clinical observation implicating abnormal retention of ammonia to the neurologic manifestations of hepatic coma was reported by McDermott and Adams in May 1953[9]. These workers studied a patient with a normal liver who had had an Eck fistula produced during an operation for carcinoma of the pancreas. This was the first time such an anastamosis (portal vein to inferior vena cava) had been produced in a patient who did not have either liver disease or an established collateral circulation. The patient's convalescence was punctuated by episodes of impaired consciousness varying from stupor to deep coma. Distinct and reversible EEG changes occurred. The episodes could be precipitated by giving ammonium salts, urea, or a high protein diet. The only consistent biochemical abnormality was in the blood ammonia which rose sharply with each episode of stupor. A low protein diet, and sulfonamide drugs to supress

TABLE III

ANALYSIS OF 35 EPISODES OF COMA IN 30 PATIENTS WITH PROVEN CIRRHOSIS

Cause	Lived	Died	Total
Primary (No known precipitating cause)	4	10	14
Secondary to:			
Hemorrhage	2	13	15
Pneumonia	0	2	2
Operation	0	1	1
Overdose paraldehyde	1	0	1
Following Paracentesis	0	2	2
	7*	28	35

*5 of these 7 died in a subsequent coma episode. Only 2 patients survived and were discharged from the hospital (Patient with overdose of paraldehyde, and 1 primary coma).

urea-forming organisms in the intestinal tract afforded protection against the spontaneously occurring episodes.

Walshe has emphasized the role of disordered amino acid metabolism, particularly that of glutamic acid which is the only amino acid oxidized by the brain. Glutamic acid binds ammonia to form glutamine which is then metabolized without liberating ammonia. Because of the apparent relationship of glutamic acid to brain and also hepatic metabolism and its relationship to ammonia which is rather consistently elevated in hepatic coma, Walshe gave glutamic acid to three patients during five episodes of coma. On each occasion there was a return of consciousness closely following administration of this agent. In one instance partial failure of this treatment may have been associated with simultaneous administration of an ammonium containing ion-exchange resin.

Implication of an abnormality in ammonia metabolism as an accompaniment of hepatic coma, appears highly probable as a result of all these studies. The

clinical implications seem to be clear. Ammonium containing drugs should be avoided, and a too high protein intake should be prescribed with caution.

In Table III, 35 episodes of coma have been analyzed from the viewpoint of cause and of prognosis. There were thirty patients in the group. Thus five patients had two episodes of coma. These patients recovered from the first one, remained out of coma for a period of time, but again developed coma from which they died. Two patients recovered and were later discharged from the hospital. One of these had been given large doses of paraldehyde. This appeared to have precipitated deep coma from which he gradually recovered when the drug was withdrawn. The other patient developed coma without a known precipitating cause.

Fourteen of the 35 episodes of coma developed without obvious precipitating cause other than advanced cirrhosis, usually with jaundice. Most of these patients entered the hospital on the verge of coma and died within a few days. Twenty-one of the episodes were directly traceable to a precipitating cause, usually hemorrhage. Shock and anoxemia from hemorrhage are known to produce temporary liver damage in individuals with a normal liver[10]. Thus a patient with advanced cirrhosis who has a hemorrhage from ruptured varices or other causes is likely to develop liver failure rapidly.

Infection is a common precursor of coma in cirrhosis, but was the precipitating factor in only one patient in this series. Another patient had an operation which precipitated it. As is well known surgery is poorly tolerated by patients with liver disease. In two the coma followed a paracentesis. This has also been noted by Karl et al[11]. Nelson, Rosenbaum and Strauss[12] found that after a paracentesis for ascites in cirrhosis, hyponatremia occurred, and that symptoms of weakness and mental confusion sometimes developed.

Drugs such as opium derivatives, barbiturates and paraldehyde, being chiefly detoxified in the liver, are poorly tolerated by most patients with reduced hepatic reserve. Coma may follow their administration. Whether this is hepatic coma or merely the effect of overdosage of a sedative drug through faulty metabolism of the drug, is a moot point. In fact coma occurring in patients with severe liver disease may not always be so-called hepatic coma (assuming this is a distinct entity biochemically), but in some cases may be coma caused by electrolyte imbalance, by drug poisoning, or even by a subdural hematoma (as noted in one of our autopsy cases in whom the clinical diagnosis had been hepatic coma).

What is the prognosis of hepatic coma? While usually fatal it is not always so. If a precipitating cause, such as hemorrhage or infection, is present and can be controlled early the patient may recover. Vigorous treatment with intravenous glucose, control of electrolyte balance, maintenance of nutrition with tube feeding, cortisone, and possibly intravenous use of glutamic acid as suggested by Walshe, may result in more recoveries.

Hemorrhage

Massive hemorrhage from the upper alimentary tract occurred in thirty five per cent of 118 cases of cirrhosis in the clinical series, there being 46 hemorrhages in 41 patients. It was responsible for death in 30 patients either as the result of exsanguination or by precipitating hepatic coma. In the autopsy series, comprising 44 patients, hemorrhage caused death in 13 patients.

One should not assume that massive hemorrhage in patients with cirrhosis is necessarily due to bleeding esophageal varices. Lipp and Lipsitz[13] reported four fatal cases of hemorrhage in Laennec's cirrhosis in whom the source of bleeding was found to be a peptic ulcer at postmortem examination. Palmer and Brick[14] studied 59 patients with cirrhosis who had a history of hemorrhage. 39 per cent had one or more lesions of the upper gastrointestinal tract, in addition to varices, which could have been responsible for the hemorrhage.

TABLE IV

Analysis of 46 Observed Episodes of Hemorrhage in 41 Patients with Proven Cirrhosis

Thirteen patients survived the first observed episode but five of these died in a subsequent episode of bleeding.

Cause of Hemorrhage	Total	Per Cent
Esophageal varices	35	76.1
Peptic ulcer	6	13.0
Hiatus Hernia	1	2.2
Gastritis (Proved, Gastroscopy)	1	2.2
Not determined	3	6.5
Total	46	100.0

In Table IV the causes of hemorrhage in 46 episodes of bleeding in 41 patients with proven cirrhosis are analyzed. Only episodes of bleeding requiring hospitalization at this hospital are included. Thirty-three of these patients died after one or more episodes of hemorrhage and all were examined postmortem. The diagnosis in the remainder was based on operation or gastrointestinal roentgenograms, gastroscopy and esophagoscopy. Bleeding esophageal varices were responsible for 76.1 per cent of the observed episodes of hemorrhage, other lesions of the upper gastrointestinal tract for 17.4 per cent, and in 6.5 per cent of the episodes the source of bleeding was not determined. Bleeding peptic ulcer occurred six times (13 per cent) in five patients. Three of these patients died and one had an emergency gastric resection to control hemorrhage. In two patients demonstrated to have bleeding esophageal varices at postmortem examination nonbleeding peptic ulcers also were present.

It is frequently stated that peptic ulcer is more common in patients with cirrhosis than in the population as a whole. Nevertheless, the incidence of peptic ulcer in cirrhosis has been noted to vary between 1.8 per cent and 19.5 per cent, depending on the type and source of material studied[15]. In one postmortem

survey[13] the authors found evidence of ulcer in 11.5 per cent of 130 cases of fatal cirrhosis while 6.6 per cent of 1,000 "control" cases had evidence of peptic ulceration. The occurrence of peptic ulcer in 625 consecutive autopsies at this hospital in 1949 was studied. Ulcer occurred in seven (15.2 per cent) of 44 patients with cirrhosis and in 64 (11.0 per cent) of 581 patients without cirrhosis. The difference is suggestive, but not statistically significant (P=0.06).

This case material was not studied from the viewpoint of the ultimate prognosis of hemorrhage from esophageal varices. Ratnoff and Patek[15], however, reported that forty per cent of 106 patients with cirrhosis and hematemesis died within one month of the first hematemesis. Another thirty per cent died by the end of the first year. Thereafter only a few deaths occurred indicating that there is a good chance of surviving two, three or four years if the patient survives the first year. Ratnoff and Patek commented that many of the patients who died early had other signs of liver failure and that the episode of hematemesis appeared suddenly as a coup de grâce among these other signs of impending liver failure.

Because of the extremely poor prognosis of hemorrhage from esophageal varices operative treatment is frequently advised to prevent further episodes of bleeding. As noted by Ratnoff and Patek, however, many instances of bleeding varices occur when the liver has already decompensated. This has also been our experience. These patients are, of course, poor candidates for operative treatment. Reynell[16] recently studied 26 patients with esophageal varices and hematemesis, treated for the most part with conservative therapy. Twelve patients who had no jaundice and a good serum protein level were followed 1 to 15 years. Fifty separate episodes of gastrointestinal hemorrhage occurred in these patients without a death. In 14 patients with jaundice and a lowered serum protein 12 were dead within two years. These findings require confirmation, but if confirmed, the indications for shunt operations for bleeding esophageal varices, and the significance of the reported results, may require re-evaluation.

Comment

Advances in our knowledge of cirrhosis have demonstrated that it is not necessarily a progressive disease, and that bed rest with a nutritious diet may result in recovery even when ascites has occurred. Surgery for portal hypertension appears to be successful in preventing further hemorrhage from esophageal varices. Yet cirrhosis remains a disappointing and frustrating disease to treat for a reason which has received little comment and inadequate attention. This is the factor of alcoholism which is the root of most of the cases. Alcoholism is one of the most resistant to treatment of all psychiatric or social disorders and further success in the management of this disease will probably occur only if it is discovered how to prevent and cure alcoholism.

SUMMARY

An analysis has been presented of 118 patients with cirrhosis studied clinically, and of 44 autopsy cases of cirrhosis out of 625 consecutive autopsies. The analysis was limited to the causes of death, to hepatic coma, and to hemorrhage. The significance of these aspects in the clinical course of cirrhosis has been discussed.

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TREATMENT OF CIRRHOSIS OF THE LIVER–RECENT INNOVATIONS*

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It is now some 15 years since the treatment of cirrhosis of the liver has undergone a revolutionary change. Heretofore regarded as a hopeless disease destined to progress rapidly and inexorably to fatal outcome, the introduction of dietary and nutritional management by Patek & Post[1] has stimulated research and observation responsible for the saving or prolongation of life in countless patients with cirrhosis of the liver.

Only the Laennec or portal nutritional cirrhosis of the liver will be presented in this paper and a synoptic analysis of new methods of therapy described.

Innovations in treatment have fallen into two fields, namely: 1) Medical forms of treatment and 2) Surgical forms of treatment. Each form will be presented and analyzed separately. Before discussing treatment however, it is imperative to take cognizance of two factors which determine the patient's expected response to therapy as Morrison has pointed out[2]: 1) An alcoholic or nutritional etiology places the disease in a category where liver damage is potentionally reversible; and 2) The degree of liver damage, whether early, moderately advanced, or late (terminal stage–far advanced), usually indicates the probability of recovery. The early or moderately advanced cases, characterized by considerable fatty infiltration and/or fatty degeneration of the liver, as well as fibrous connective tissue proliferation, give the best therapeutic response. On the other hand, the small, shrunken, fibrotic, "terminal" liver of Laennec invariably deteriorates to death despite any form of treatment.

Medical Treatment

1. Diet and Vitamin Supplements:—A. Dietary and vitamin supplementary therapy was first shown by Patek to arrest the progress of the disease in a significant percentage of cirrhotics and to restore many invalided patients to normal activity. In the ambulatory patient or one who is able to take food normally, the "basic" diet consists of 150 g. protein, 400 g. carbohydrate and 100 g. fat, the dietetic "goal". Whenever possible the patient should be encouraged to exceed this intake to shorten the morbidity period. Alcohol is strictly prohibited; eggs should be eaten once to twice daily; meat at luncheon and supper; and milk drunk throughout the day, drinking a minimum of six glasses. Where the patient is unable to ingest a "solid" diet, a semi-liquid diet may be employed, utilizing the strained or pureed meats as processed in baby foods, jello and gelatines, eggnogs, pureed vegetables, strained cereals, powdered

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milk drinks, each containing one to two tablespoonsful of flavored brewer's yeast or Vitamin B-complex substitutes, together with a vitamin supplement containing all synthetic vitamins in a potent form.

B. If the patient is unable to eat or is comatose, tube feeding of nourishing concentrates may be used as soon as possible where esophageal bleeding is absent, using a small nasogastric tube. Protein and carbohydrate mixtures, each 150 g. in 2 liters of liquid are easily prepared and administered, utilizing such mixtures as 200 g. of skimmed milk powder, 20 g. each of cocoa and sugar and a quart of whole milk. Predigested amino-acid preparations combined with carbohydrates are also available by numerous pharmaceutical houses.

2. *Parenteral Therapy:*—Where the patient is comatose, parenteral administration of blood and/or intravenous administration of 5 to 10 per cent continuous glucose drip as introduced by Snell and Butt[3] is highly recommended. They gave 3 to 4 liters daily with 50 to 100 mg. thiamin chloride and 250 to 500 mg. of nicotinic acid. Greatest caution, however, must be exerted to constantly observe blood electrolyte balance in order not to precipitate or aggravate coma from excessive parenteral glucose therapy. Vitamin K in daily 72 mg. doses is administered always in the presence of hypoprothrombinemia, and the subsequent response of blood prothrombin levels is often a useful prognostic guide. Vitamin B_{12} intravenously or intramuscularly in 20 mcg. doses daily may also be utilized as a useful lipotropic agent as suggested by Gyorgy's work[4].

3. *Serum Albumin:*—The author has not found serum albumin to be valuable and is aware of its production of fatal hemorrhage[5] or pulmonary edema[6], as well as its inability to improve liver function[7] or to reduce ascites or produce diureses. I have not used parenteral amino acids in the presence of severe liver damage in view of the toxic results which occur when the liver is unable to deaminize proteins.

4. *Electrolyte balance* has recently assumed major importance in treatment. As Eisenmenger[8], Ralli[9] and others have shown, patients with cirrhosis retain salt and demonstrate impairment in renal sodium excretion irrespective of the salt intake thus influencing the formation of ascites and edema. Hence the present concept of a low salt diet (200-600 mg. daily) to combat ascites and edema. The dangers of a low salt syndrome uremia and coma are now well known if too rigorous salt restriction is induced or associated with excessive use of mercurial diuretics and ammonium chloride. When used carefully, however, parenteral mercuhydrin in 2 c.c. doses injected intramuscularly twice weekly has been useful in treating ascites.

5. *Resins:*—The recent introduction of cation exchange resins for edema and ascites in cirrhosis of the liver has opened a new therapeutic avenue of approach, but one which is still fraught with serious hazards and complications. Following personal experience the author therefore believes that it is to be used only where: (a) the dietary intake is entirely consumed by the patient, and (b) where

constant observation is possible so that detailed, daily studies of the patient's electrolyte balance are possible. Since adequate control of these resins does not seem to be possible for routine clinical use, they are not safe due to the clinical dangers of potassium deficiency, hyponatromia, acidosis and toxicity[10].

6. Lipotropic Agents:—Although opinion has been controversial regarding the therapeutic advantages of lipotropes in the treatment of nutritional cirrhosis of the liver, the author's experience over ten years with these substances has shown their therapeutic value when used under advantageous conditions[11]. Albeit an appropriate diet may secure similar results in the long run of treatment, the lipotropic agents do clear damaged hepatic parenchymal cells of fat most rapidly when the liver damage is "reversible" as Steigman[12], Morrison[13] and others have shown. It seems logical that when fatty degenerative changes in the liver can be cleared or corrected more rapidly in the experimental animal by the use of lipotropes, these same agents should be used in human subjects to shorten the duration of illness and to reduce the mortality rate[14]. As the author[15] has emphasized, these agents should be considered as therapeutic or dietary supplements to assist the faltering or failing liver by providing synthetic dietary bridges in the transmethylation process. Choline, betaine, liver extract and Vitamin B_{12} have been found by the author to be the most useful therapeutic combination by virtue of synergistic action, although methionine and inositol are also useful. Betaine in particular has been tolerated best of all[16]. As in the case of choline where dosages averaging 6 g. daily with the other lipotropes as supplements are given, the most effective therapeutic results have been secured. It was previously stressed in this paper that the lipotropic agents are of value only in the "reversible" case of cirrhosis where the disease has not advanced to the terminal or too far-advanced stage. The lipotropic agents are best administered orally in three divided doses daily after each meal.

7. Liver Extracts:—Parenteral use of crude liver extracts was first introduced by Labby[17], Ralli[18] and others and after some 15 years use by the author has been found to be a useful therapeutic adjunct in stimulating hepatic parenchymal tissue regeneration, improving appetite (via the so-called "appetite stimulating factor"[17]) and by reduction of antidiuretic hormones. The lipotropic effect of crude liver extract in experimental animals has already been demonstrated[19]. Intravenous liver extract has also been advocated by various observers, but we have discontinued its use following death due to its use in one of our patients and anaphylactic shock in several other of my patients. We have used from 1 to 3 c.c. crude liver extract intramuscularly daily, every other day or twice to once weekly in patients with satisfactory results, depending on the severity of the disease and the clinical indications. If desired, the liver extract can be combined with 10 to 30 mcg. parenteral Vitamin B_{12} and/or Vitamin B-Complex since lipotropic effect has been ascribed to these latter two vitamin preparations which can also be administered through the intravenous route if indicated, together with Vitamin K and/or Vitamin C.

8. Cortisone and ACTH:—Most reports concerning the use of these steroid hormones have been discouraging in the treatment of cirrhosis[27]. The author has had three patients in whom aggravation of the disease occurred, particularly in the precipitation of ascites and jaundice. It is possible, however, that rigid salt dietary control and critical reduction of sodium intake was not satisfactorily effected in my cases. Some reports as those by Zoeckler and Hegstrom[28] or Helm[29] have been enthusiastic about the therapeutic value of cortisone for cirrhosis. The author feels that cortisone should not be employed therapeutically unless every other therapeutic device has been exhausted and the patient's condition is deteriorating significantly. Cortisone could then be used with careful attention to sodium restriction and electrolyte balance, using doses of from 100 to 200 mg. daily for two weeks as a trial period, and employed subsequently according to therapeutic response. Other hormonal treatment such as methyl testosterone propionate has not resulted in the routine use of androgens for cirrhosis.

Surgical Treatment

1. Although balloon tamponage for the control of hemorrhage from esophageal varices is not a surgical procedure in the strictest sense, its use has been introduced by surgeons Sengstaken and Blakemore[21], and it has proven to be of great value in this regard. It has thus often been possible to control variceal hemorrhage while high protein, high vitamin nutrient feedings are administered through the nasogastric Sengstaken tube. While the balloon is *in situ* controlling and arresting hemorrhage, blood transfusions are administered to bring the hematocrit to 40 per cent; intravenous glucose and vitamin supplements are given to an adequate fluid requirement of some 4,000 c.c., daily. Usually the Sengstaken balloon can be removed safely in several days and semi-solid feedings can be given orally, with supportive therapy such as intramuscular crude liver extract, etc. In most cases of repeated esophageal or gastric varices bleeding, one week of this regime is enough to prepare the patient for a portacaval shunt. In the author's opinion this should be carried out in most cases of massive gastric or esophagovariceal hemorrhage since this is the most serious complication of portal hypertension in cirrhosis of the liver.

2. Portacaval shunt:—The creation of an internal fistula, i.e.: an anastomosis between the portal vein and the inferior vena cava, as advocated by Blakemore[22], has been the best surgical approach for portal hypertension with massive hemorrhage due to gastric or esophageal varices. In patients with an extrahepatic portal block, best results have been obtained by splenectomy with splenorenal shunt as carried out by Rousselot[23] and Linton[24]. Since the author is not a surgeon the reader is referred to the above mentioned surgical innovators for further surgical details.

3. Other surgical procedures:—Briefly mentioned are: (a) the new procedures of mediastinal packing for bleeding esophageal varices associated with portal hypertension as introduced by Garlock[25]; and (b) ligation of the hepatic

and splenic arteries for ascites by Rienhoff and Woods[26]. Since these are completely new procedures, sufficient time has not elapsed to permit their critical evaluation. Abdominal paracentesis is indicated for ascites which embarrasses respiration or produces distention that interferes with appetite or food ingestion.

Rehabilitation:—The after care of the cirrhotic patient is perhaps the most critical aspect of his case, following recovery from the acute exacerbation of his illness. Since we are discussing the most frequently occurring form of cirrhosis of the liver, the alcoholic, nutritional type of Laennec's cirrhosis, the psychiatric aspects of each case will usually determine the future progress and prognosis of the disease. Practically all texts or papers on the subject of cirrhosis of the liver reviewed by the author do not touch on this phase of the disease. And this is not surprising in view of the fact that such an authority as Menninger[20] has reported failure in the majority of alcoholic patients who underwent psychotherapy in the attempt to cure their alcoholism. A minority of patients, however, have shown a satisfactory response to psychotherapy. A substantial group of patients also have responded to the kind of lay psychotherapy and intimate personal relationship, inspiration and "revivalist" rehabilitation afforded by "Alcoholics Anonymous". "AA" has unquestionably succeeded in innumerable instances of alcoholism under the author's care and deserves more recognition by the medical profession as a valuable form of "group therapy".

Summary and Conclusions

1. Therapeutic medical and surgical innovations for the treatment of nutritional cirrhosis (Laennec) of the liver have been reviewed and analyzed. These advances have been responsible for the reduction of morbidity and mortality rates in this disease.

2. The best results from treatment have been secured in the early or moderately advanced cirrhosis where "reversibility" of hepatic parenchymal damage is present.

3. The most effective medical treatment has centered about:

a) High protein (150 g.), high carbohydrate (400 g.), moderate fat (100 g.) diet intake in the ambulatory patient. Where possible this caloric intake is exceeded. When the patient cannot ingest this diet, modified oral and/or parenteral feedings are described.

b) Vitamin supplements, brewer's yeast and other nutrients such as amino acid preparations which are valuable dietary adjuncts.

c) Maintenance of a normal electrolyte balance, especially in the presence of ascites and edema. The advantages of a low sodium dietary intake and the dangers of the "low salt syndrome" are emphasized. Cation exchange resins to control ascites and edema are still under observation.

d) Lipotropic agents such as betaine (6 g. daily), and/or choline (6 g. daily) with liver extract and Vitamin B_{12} are proven valuable aids to therapy as dietary supplements for reduction of morbidity and mortality rates in cirrhosis.

e) A psychological rehabilitation program in the after care of the alcoholic patient is stressed utilizing psychotherapy and "Alcoholics Anonymous".

4. Surgical treatment is outlined and is comprised mainly of the control of massive variceal hemorrhage by the Sengstaken balloon and/or by portacaval shunts.

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PATHOLOGIC-PHYSIOLOGICAL ASPECTS OF CIRRHOSIS OF THE LIVER*

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My task in this symposium can only be a short survey of the altered physiology in cirrhosis of the liver inasmuch as its understanding helps the clinician to evaluate the significance of symptoms, signs and laboratory tests, and to arrive at a sensible rationale of the treatment of this disease. It is beyond our scope to discuss the etiology, pathogenesis, classification and histological details of various types of hepatic cirrhosis. It is sufficient for our purpose to analyze the functional consequences of hepatic cirrhosis which generally is defined as *combination of parenchymal cellular damage* with *proliferation of connective tissue,* and usually with *reparatory regeneration of liver cells.*

It is clear from this definition that we have to expect altered physiology due to the interference of the newly formed and shrinking connective tissue with (1) the blood circulation within the liver and (2) with the biliary flow; (3) the primary hepatocellular damage will be associated with disturbance of function.

1. The blood circulation within the liver is greatly influenced by the proliferative process of the connective tissue with subsequent contraction and by postnecrotic scarring of the parenchyma. Distortion and obliteration of small vascular branches affect first the thin-walled vessels carrying blood under relatively low pressure, that is, the capillaries and ramifications of the portal vein. This will occur particularly if the proliferation of the mesenchyma sets in from the interlobular septa containing the vascular bed, that is, in so-called "portal cirrhosis" or "Laënnec's cirrhosis". The obvious result of this process will be increased resistance to the portal blood stream and hence elevated blood pressure in the portal vein. This elevation will be enhanced by increased blood flow through anastomoses to intralobular sinusoids from arterial capillaries and arterioles of the hepatic artery system whose pressure is considerably higher than that of the portal vein system. These arteriovenous anastomoses are used in various degrees under normal conditions.

There is no unanimity about the normal pressure in the portal vein. First it was found to be on the average 65 mm. H_2O (=4.8 mm. Hg.) and in the hepatic veins 0 to 10 mm. H_2O[1]. Later much higher figures have been reported (150-220 mm. H_2O) from direct measurements at operations[2]. Indirect measurements by cardiac catheterization and blocking a branch of the hepatic vein yielded a pressure of 6.8 mm. Hg. (=92 mm. H_2O) which compared favorably

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to values obtained by direct determinations[3]. In 11 cases of portal cirrhosis the values were raised to 22 mm. Hg. (=300 mm. H_2O). In some cases of hepatic cirrhosis figures as high as 400 mm. and even 600 mm. H_2O have been found by other investigators[4].

This situation involves important implications. (a) The impairment of blood flow from the portal vein through the liver and the elevated pressure within the portal veins brings about increased flow through preexistent *collaterals* and formation of new ones connecting the portal system with the inferior cava. Hence the engorgement of the dilated veins of the anterior body wall and the formation of the dreaded *esophageal* and *gastric varices* with the impending danger of massive hemorrhage. In the distended veins of the upper abdomen the blood flows upwards into the thorax, and in the lower abdomen down toward the femoral vein in the groin. The diagnostic importance of the so-called caput Medusae consisting of clustering veins around the umbilicus lags far behind its fame. It can develop only if the fetal umbilical vein remained patent instead of being obliterated.

(b) The intrahepatic vascular obstruction and elevated pressure in the portal vein leads to *passive congestion of the spleen* with enlargement and possible functional impairment of this organ. Anemia of various types, leukopenia and thrombocytopenia are known to occur in cases of cirrhosis of the liver. Whether or not hypersplenism might be involved in the pathogenesis of such alterations of the cellular blood elements in certain cases of cirrhosis requires further studies. Eppinger's[5] experience with splenectomy in a small group of selected cases of cirrhosis is at least suggestive of such a possibility. Splenectomy also may diminish or even obliterate esophageal varices. Furthermore, it has been found that regeneration of experimentally damaged liver in animals is enhanced by splenectomy[5].

(c) Although portal hypertension alone cannot account for the formation of *ascites* there cannot be any question that it must be considered as a contributory pathogenetic factor.

(d) Since only the intrahepatic circulation of the portal blood becomes impaired first, the blood supply of the liver from the hepatic artery will be changed. It has been shown that any decrease or increase of the circulating blood volume in the portal system is accompanied by an opposite alteration of the blood volume passing through the *hepatic artery*. The classical perfusion experiments of McIndoe[6] on cirrhotic livers demonstrated that 86-100 per cent of fluid injected into the portal vein passed into collateral channels rather than into the hepatic vein. A much higher percentage of the injected fluid returned through the hepatic vein if the perfusion was carried out through the hepatic artery. Measurements of the blood flow through the liver of dogs (with the Stromuhr of Rein) revealed that 12 to 25 per cent of the blood comes from the hepatic artery. This blood loses 50 per cent of its O_2 until it leaves the hepatic vein; the venous

blood of the portal vein gives off 20 per cent of its O_2. This means that 40-45 per cent of the oxygen is supplied to the liver by the hepatic artery and 55-60 per cent by the portal vein[7]. If the portal blood supply is shut off to a large extent in portal cirrhosis the oxygen supply of the liver depends far more on the hepatic artery.

It is therefore obvious that *ligation of the hepatic artery* in portal cirrhosis is an extremely risky procedure. In normal dogs it results in necrosis of the liver parenchyma. It is understandable that ligation of hepatic and splenic arteries stops an acute hemorrhage from esophageal varices secondary to cirrhosis of the liver, but it is likewise to be expected that a fatal outcome might ensue[8].

Recently it was shown[9] that in hepatic cirrhosis an extensive vascular network forms in the septa to which the hepatic arteries also contribute blood and that this network is drained by branches of the hepatic veins. By this process the blood is shunted from the portal to the hepatic veins and bypasses the sinusoids of the liver parenchyma. It represents a kind of internal Eck's fistula. This is another factor that contributes to the progressive destruction of the liver cells.

(e) The alteration of circulation through the cirrhotic liver results in partial *bypassing the liver* of blood from the radicles of the portal vein, that is from the intestines, the spleen and the pancreas. Thus certain substances originating from these organs fail to be modified (*detoxicated*) instantly in the liver as they are under normal circumstances. Phenolic compounds such as indol and scatol are formed in the intestines by putrefaction of amino acids and are conjugated in the liver with sulfate and excreted in the urine as ethereal sulfates. Aromatic acids are combined with glycine, other substances with glucuronic acid, glutamine or acetic acid. Certain substances foreign to the body are destroyed by oxidation in the liver such as strychnine and nicotine or certain barbiturates. No special data are available to my knowledge as to the clinical consequences of the insufficient hepatic detoxication of portal blood in cirrhosis of the liver. Do such consequences of bypassing the liver by portal blood occur in hepatic cirrhosis if intestinal putrefaction is excessive; does hypersensitivity of such cirrhotics exist to salicylic acid or pentobarbital taken by mouth? We do not know either whether splenic and pancreatic hormones undergo modifications in the liver and act differently if they bypass the liver.

A number of liver function tests, however, have been recommended that are based on the "detoxifying" function of the liver. Camphor, menthol, salicylic acid and other substances were tried for this purpose and later abandoned. Only the *hippuric acid test* (conjugation of benzoic acid with glycine) is frequently used as an indicator of hepatic function if impaired renal function can be ruled out. In cases with impaired portal circulation it may indicate as well partial bypassing of the liver rather than a functional defect of the liver cells. The same holds true for abnormal amounts of *urobilinogen in the urine* of cirrhotic patients with impaired portal circulation.

(f) The *retardation of the portal blood flow* in cirrhosis of the liver is thought to be responsible for the frequent occurrence of meteorism, flatulence and "gas pain" which often usher in the clinical picture of the disease. Intestinal gas is said to be less readily absorbed from the circulating blood in the intestinal wall if the circulation is retarded.

(2) *The biliary flow* within the cirrhotic liver may be impaired in various ways. This will occur particularly but not exclusively if the proliferation of connective tissue extends into the lobules and starts from the smaller bile ducts and canaliculi. Cases of this type have been classified in the older literature as *Hanot's hypertrophic biliary cirrhosis* with jaundice and splenomegaly but without ascites. Today we better speak of *cholangiolitic cirrhosis* which designates both the inflammatory character and origin of the cirrhotic process from the small bile ducts. Obliteration of bile capillaries by inspissated bile and bile thrombi are seen on microscopic examination. Rupture of biliary ampullae at the periphery of lobules or of intralobular bile ducts, abnormal communications between bile capillaries and the lymph spaces of Disse due to swelling and necrosis of liver cells may cause intrahepatic regurgitation of bile and consequently jaundice. Bilirubin in this type of intrahepatic regurgitation jaundice will give a prompt direct reaction in the Hijmans van den Bergh test.

It stands to reason that bile salts likewise reach the systemic circulation under these circumstances if, and as long as the liver cells are capable of synthetizing them. Pruritus of jaundiced patients is believed to be due to irritation of sensory nerve endings by bile salts. It is not often seen in cirrhotics because the hepatocellular damage prevents their manufacture in sufficient amounts as contrasted with extrahepatic regurgitation icterus.

(3) *The hepatocellular damage* is probably the primary factor in the pathology of most cases of hepatic cirrhosis. Nature provided us with an abundance of reserve power with regard to the function of the liver parenchyma. More than 80 per cent of it must be damaged in order to be detected by our clinical liver function tests. The extension of damage is more important than its intensity. Furthermore, the great regenerative tendency of the liver leads to nodular hyperplasia of liver cells. This factor, however, is probably of minor functional importance because of disorganization of the newly formed lobules which lack normal blood supply due to distortion of the portal vessels by proliferating connective tissue. Hence they do not contribute much to functional adequacy of the cirrhotic liver. The functions of the liver are so numerous that no one single clinical test can be expected to reflect the general functional adequacy of the organ.

(a) The disturbance of *the excretory cellular function* of the cirrhotic liver is of less clinical importance than the disturbance of its metabolic functions. Bilirubin-globin produced by the reticulo-endothelial system (RES) and reaching the liver cells with the blood stream is split and free *bilirubin* excreted into biliary capillaries even in biliary and portal cirrhosis. Quantitative diminution

of this function, however, may occur. Only in exceptional cases of far advanced atrophic portal cirrhosis the stools may be clay-colored, and the biliary ducts found patent. Positive delayed or indirect bilirubin reaction of van den Bergh indicates this state of cellular failure to free bilirubin from its protein compound.

Contrariwise, the failure of the liver cells to remove from the portal blood all the *urobilinogen* in order to re-excrete it as bilirubin is an early sign of hepatic insufficiency. Considerable urobilinogenuria is, therefore, a very important clinical test of liver function if there is no complete biliary obstruction and no increased destruction of red blood corpuscles.

Bile salts are formed in the cirrhotic liver usually at least in sufficient quantity not to impair significantly the absorption of fat and fat soluble vitamins from the intestine. Besides microscopic or chemical examination of the stool serial testing for chylomicrons in the peripheral blood after a fat meal is a suitable method to determine intestinal fat absorption.

There is no doubt, however, that the excretory function of the liver may be greatly impaired in cases of cirrhosis if evaluated by clinical tests. The most physiological of those tests is intravenous injection of a bilirubin solution and determination of its retention in the blood after a certain time. The most popular test is the well known sulfobromophthalein (bromsulfalein) test. Many other dyes have been used for the same purpose. Failure of visualization of the gallbladder on cholecystography may be due to deficient excretion of the dye by the liver cells.

(b) Disturbances of the manifold *incretory* (*metabolic*) *functions of the liver cells* are quite common in cirrhosis of the liver.

The protein metabolites absorbed from the intestine reach the liver as *amino acids*. They are partially deaminized and converted into ammonia and urea; partially they are used for synthesis of proteins. Increased amino acids in the plasma of cirrhotics are indeed found in far advanced, usually terminal cases. Millon's reaction in the urine is a very simple and convenient test indicating the presence of tyrosine and related oxyphenol compounds. Crystals of tyrosine and leucine may be found in the urinary sediment. Simultaneously the urea-N will be found low and the so-called "residual N" (this is NPN minus urea-N) increased.

The *synthesis of proteins*, especially albumin, fibrinogen, prothrombin and cholinesterase may be greatly disturbed in cases of hepatic cirrhosis. Especially decreased albumin with increased globulin fractions is often found in early cases of cirrhosis. Even more so are the various *flocculation tests* which depend on more delicate alterations of the protein composition of the blood serum. The results of those tests are not always concordant because they depend on different alterations of the protein mixture and serum lipids.

From the viewpoint of clinically disturbed physiology the *diminution of albumin* is the most important alteration. Because of the relatively much smaller

molecules of albumin as compared with globulin the osmotic pressure of the blood plasma will be lowered by hypoalbuminemia. Hence the tendency to edema and, particularly if the pressure in the portal capillaries increases, to *ascites.* Neither hypoalbuminemia nor portal hypertension alone or their combination, however, is a sufficient explanation of the pathogenesis of ascites. Other contributory factors are probably increased capillary permeability, increased antidiuretic factor and renal retention of Na.

The fact that the protein content of the ascitic fluid was found to vary between 0.1 per cent and 3.8 per cent[2] indicates that the capillary walls may be permeable for colloids in variable degree. This is corroborated by the fact that free exchange between the blood plasma and the ascitic fluid has been demonstrated by using radioiodinated serum albumin[10].

Since Elaine Ralli reported increased amounts of an antidiuretic factor in the urine of cirrhotics a large controversial literature developed on this subject[4]. It is not yet settled whether this antidiuretic factor is identical with the posterior pituitary hormone, and if so, whether it is not sufficiently inactivated by the cirrhotic liver or produced in excess by the pituitary. Recently it was even found that the antidiuretic factor of human serum is not increased at all in cases of portal cirrhosis and cannot be identified as posterior pituitary hormone[11].

Failure of the kidney to excrete Na in normal amounts was interpreted as a result of excessive quantity of adrenal corticoids perhaps not sufficiently inactivated by the cirrhotic liver. A low Na content of sweat and saliva found in such patients seems to corroborate this concept[4]. Rats and pigs at least possess a hepatic enzyme system that transforms various cortico-adrenal steroids into compound which is the physiologically most active and important product F[12]. One might, therefore, expect diminution of corticoadrenal effects rather than diminished "inactivation" of cortical products in failing liver function. This, of course, is only a hypothetical assumption. Symptoms or signs of adrenal cortical hyperactivity are lacking in patients with hepatic cirrhosis.

Whatever the mechanism may be that is operative in producing water and Na retention in patients with hepatic cirrhosis, the *water retention* in hepatic parenchymatous lesions has been known for 50 years. Oliguria and delayed elimination of 1,500 c.c. of water or weak tea for a period longer than 4 hours is a characteristic, though not specific sign of parenchymatous liver disease. That it is also observed in cases of adrenal insufficiency is somewhat at variance with the above mentioned hypothesis of insufficient inactivation of adrenal corticoids by a damaged liver. A diuretic hormone produced by the liver had been assumed by E. P. Pick[13] but was questioned by later investigators. Na as well as Cl and bicarbonates are physiologically retained to a certain degree by the liver and excreted with the bile[7]. This mechanism deserves consideration also. S. Wright[2] mentions that for unknown reasons a diet rich in meat and even protein-free extracts of meat increase the tendency to ascites in cirrhosis of the liver.

Inactivation by the liver has not only been assumed for the posterior pituitary hormone and adrenal cortical hormones but also for progesterone and androgens, and has been definitely proven for *estrogens*. B. Zondek[14] elaborated an "estrone clearance test" for hepatic function. It is conceivable that testicular atrophy and gynecomastia in some cases of cirrhosis develop on this basis. Lack of hair on the chest and female (juvenile) arrangement of pubic hair in many male cirrhotics, however, is usually preexistent and constitutional in type rather than acquired in the course of cirrhosis. I hesitate to share the opinion of those who explain the spider angiomas and palmar erythema of cirrhotics by deficient inactivation of estrogens. Recently such spider angiomas were reported following use of adrenocorticotropic hormone[15].

Decreased *prothrombin*, a glycoprotein, in the blood plasma is a frequent sign of hepatic insufficiency in advanced cases of cirrhosis if Vitamin K is available to the liver. Hypoprothrombinemia contributes to the hemorrhagic tendency of severe cases.

Cholinesterase is believed to be synthetized in the liver in parallel with albumin. Consequently the serum cholinesterase is diminished in parenchymatous liver diseases including cirrhosis. It is normal in uncomplicated obstructive jaundice[16].

The liver is the *storage place of glycogen* and herewith the target organ of all the hormones and the sympathetic nervous system involved in the maintenance of normal blood sugar. Glycogenesis from deaminized aminoacids and fatty acids of fat on one hand, and liberation of glucose (glycogenolysis) if the blood sugar level decreases, on the other hand, are functions of the liver performed with an array of enzymes and securing the homeostasis of blood sugar. It is understandable that this vital function of the liver is disturbed only in extensive destruction of the liver parenchyma. Fasting *hypoglycemia* below 60 mg. per cent has been found in only 2 per cent; below 50 mg. per cent in only 1 per cent of cases of hepatic disease[17]. It must be conceded, however, that transient hypoglycemia frequently might be overlooked or its symptoms misinterpreted[18]. Its frequency, therefore, is probably higher. Glucose tolerance, insulin tolerance and rise of blood sugar after epinephrine are quite variable in hepatic cirrhosis and unsuitable as tests of hepatic function. Remarkable, however, are rare cases of preexistent diabetes mellitus which happen to develop cirrhosis of the liver later. Their diabetes may show a surprising improvement or disappear completely and turn into spontaneous hypoglycemia[19,20].

The utilization of different sugars for glycogenesis depends on different enzymes. Among the various hexoses, galactose is removed from the blood exclusively by the liver whereas other hexoses are taken up by other organs also. Therefore the *galactose tolerance test* represents a valuable indication of liver function and demonstrates impairment of this function in cases of hepatic cirrhosis.

The liver plays an important part in the *intermediary metabolism of fat and lipids* by desaturating fatty acids and reshaping the fats for storage in fat depots and by breaking them down to ketone bodies which, in turn, are used up in other tissues. No significant clinical consequences of an impairment of these functions, however, are known to occur in cirrhosis of the liver.

The metabolism of *cholesterol* and *phospholipids*, though not yet sufficiently elucidated, is intimately connected with the liver function. To a large extent these lipids are synthetized in the liver and the esterification of cholesterol in particular depends on the function of the liver cells. Hence the elevation of blood lipids in obstructive jaundice which prevents the physiological excretion of cholesterol with the bile; hence also the drop of phospholipids and cholesterol, especially cholesterol esters in severe parenchymatous hepatic disease. Patients with cirrhosis may, therefore, present different figures of their blood lipids dependent on type and stage of the cirrhotic process. In cases of biliary cholangiolitic cirrhosis with or without xanthomatosis cholesterolemia may be extremely high. The possibility has been considered that cholesterol is not only not eliminated through the bile but that it might be synthetized in excess by the liver[21].

Clinical manifestations of *vitamin deficiency* as a consequence of hepatic cirrhosis are not frequent although the liver is concerned with storage and, to a certain extent, with chemical transformation (methylation of nicotinic acid) of vitamins. Elevated blood levels of pyruvic acid are frequently found in hepatic cirrhosis. Metabolization of pyruvic acid depends on the presence of thiamine which acts only in phosphorylated form, that is, as diphosphothiamine. This phosphorylation of thiamine, however, takes place in the liver. Increased amounts of pyruvic acid in the blood may indicate, therefore, hepatic dysfunction and deficiency in active thiamine for utilization by the tissues[22].

Alkaline phosphatase is produced by the bones and excreted in the bile. Any obstruction of bile flow or cellular failure to excrete the phosphatase raises therefore the level of alkaline phosphatase in the blood. Some authors believe that this enzyme is also made by the liver. Consideration of these facts explains the different results of this test obtained in cases of hepatic cirrhosis.

The functions of the liver concerned with the storage of the *anti-anemic principle* and of *iron* (as ferritin), with *copper* metabolism (in hepatolenticular degeneration of Wilson) and with regulation of the *ionic equilibrium* of the body (retention of Na, Cl and bicarbonate) may become disturbed in liver cirrhosis but do not play a significant part in its clinical picture.

It stands to reason that advanced cirrhosis of the liver with serious impairment of its many functions must have a repercussion on the function of *other organs*. This is particularly the case as far as the gastrointestinal tract, the kidneys (hepatorenal syndrome), the circulatory system and the central nervous system are concerned. The heart muscle suffers by the alteration of the blood proteins (Wuhrmann's *myocardosis* due to dysproteinemia[23]); the blood pressure

may be influenced by alteration of ferritin which exerts a vasodepressive action (*vasodepressor material* of E. Shorr et al[24]); the brain function is highly sensitive to hypoglycemia.

Of special interest is the *enlargement of the spleen* in many cases of cirrhosis. Portal hypertension and passive congestion accounts only for one group of cases. I gained the impression that considerable splenomegaly develops particularly in those cases of hepatic cirrhosis that are secondary to infectious hepatitis. This would be in accord with Himsworth's[25] opinion that reticular hyperplasia of the spleen results from products of degenerating and necrotic liver cells which are carried to the spleen by the blood stream. Experimentally induced liver damage in animals induces reticular hyperplasia and splenomegaly even if the spleen has been transplanted in the abdominal wall and all vascular connections with the portal system have been severed. In cholangiolitic cirrhosis the infectious factor may act simultaneously and directly upon the spleen. In a small group of "splenomegalic cirrhosis" with dark bile and intensely colored feces a hemolytic component has been assumed by Eppinger[5], who recommended splenectomy for such selected cases.

Considering the many vital functions of the liver it is amazing to what large extent the liver parenchyma may be destroyed before the fatal outcome is announced by the appearance of *cholemia* or *hepatic coma*. This clinical picture is the result of a break-down of various hepatic functions in different degree and combination. Renal failure, hemorrhagic diathesis, deprivation of the brain of vital fuel (glucose) and vitamins, poisoning by not detoxified material, circulatory collapse, blocking of various enzyme systems and other consequences of liver failure bring about this impressive tragic picture of the last and mostly fatal stage of hepatic cirrhosis.

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Discussion

Dr. Samuel Weiss (New York, N. Y.):—Because of the limited time allotted to me, I shall be brief in discussing these interesting papers.

As early as 1932-3, I called attention to certain diagnostic criteria by using infra-red photography. In private practice and in the gastrointestinal clinics I saw many patients with spider angiomas over the right diaphragmatic area, which I was unable to account for. When infra-red photography was suggested as a possible means of bringing out these superficial veins, all patients having these spider venules with or without definite liver symptoms, were photographed from time to time to watch their progress.

More than seven hundred and fifty patients, private and clinic, had come under observation and by this means I was able to formulate a diagnostic criteria. By noting the course of these superficial veins as they became engorged, gave me a clue as to the underlying pathology of the liver and its blood vessels. When these veins were more prominent on the lateral part of the trunk, it became evident that the inferior vena cava was involved. If the direction of the engorged veins were directed toward the axilla, an embarrassment of the superior vena cava was present, and if the veins were engorged on the lower part of the thorax, the syndrome of portal hypertension was entertained. At operation or autopsy the diagnosis, as a rule, was confirmed.

As to liver biopsy, it is now a routine procedure if it is done by competent and well-trained physicians who observe the necessary precautions. We do a good many of these liver biopsies in the hospital in New York. We are careful to train our interns and residents and we do not permit them to use the needle until they have had sufficient experience. I think Dr. Jankelson ably told you this morning that there is a great deal of danger in using the needle if you are not careful. Both procedures have their merits.

As to Clinical Aspects of Cirrhosis of the Liver by Dr. Halsted and Dr. Fainer which was quite instructive, I would like to call attention to the use of liver extracts intravenously which Dr. Morrison mentioned and which is also used at the New York Polyclinic by Dr. Rawls and me. We have had numerous cases without any deaths. We tested the patients as to sensitivity. If we found a patient was sensitive, no intravenous liver was given. We felt that liver extracts may be used when carefully introduced, provided there were no contraindications.

Dr. Morrison, who did a great deal of research and clinical observation on cirrhosis of the liver and arteriosclerosis, mentioned that unfortunately not all patients with cirrhosis of the liver were early cases and reversal of the process did not occur. How are you going to diagnose the early cases? Early cases when diagnosed and given an adequate diet with the minimum of fat as advocated by Drs. Morrison, Patek and others, may prevent further parenchymal damages and avert the progress of the disease. Advanced cases with ascites, however, have not been the ideal patients.

With reference to coma, Dr. Richard Bauer, formerly of Vienna, for many years advocated the use of intravenous liver injections. When he presented this before the American College of Physicians it was received quite well. It has been abandoned for a time, but I see it has been revived again. The only reason it was abandoned was because the patients died and probably the question arose as to whether the intravenous liver extract hurried their death.

In the treatment of liver coma ACTH is frequently used with more or less good results as it was pointed out by one of the speakers; some of them live and some of them die. So far we have had excellent results with ACTH.

Dr. Julius Bauer's presentation of the anatomical, pathological and physiological aspects of cirrhosis of the liver is clear and concise. I hope that when this symposium is published in our journal, it will make excellent reading matter not only for the specialist but also for the general practitioner.

Dr. Hyman I. Goldstein (Camden, N. J.):—I would like to call attention at this time to a thesis: "Du diagnostic anatomique des maladies du foie, et de sa valeur au point de vue thérapeutique" (Paris, J. B. Baillière, 1844; Félix Malteste et Cie., 1884), by Ange Gabriel Maximé Vernois (1809-1877) in which he discusses liver puncture biopsy for diagnostic purposes. Since the work of Iversen and Roholm (1939) and at the Mt. Sinai Hospital of New York (1939) and elsewhere, liver biopsy has been used for diagnostic purposes quite frequently.

I might mention here, as of historical interest, that Louis Pasteur performed liver puncture biopsy on diabetic patients in 1883—seventy years ago, for the study of the glycogenic content of liver tissue. These notes appear in the little monograph on "*Diabetes*" by Professor Fried. Theod. Frerichs (1883).

Dr. Felix Cunha (*San Francisco, Calif.*):—I would like to have Dr. Halsted, Dr. Morrison and Dr. Jankelson comment a bit on this. A five-by-five, 64-year old red-cheeked Irishman came into my office. He told me that he drank six quarts of whisky per day. I checked on it. I thought of the economic angle. He drank only bonded bourbon. That costs about $40.00 a day. His brother said, "Think nothing of it, Doctor. He doesn't have to worry about finances. He is a bachelor. He owns a patent that is sold to railroad companies, something that is used by the railroads but he doesn't even manufacture it himself."

I took all the conceivable hepatic function tests; I tested his blood sugar levels and they were all normal. He said, "Good God, Doctor. You are not going to tell me that I will have to stop drinking?" I said, "No, it would kill you." How do you account for that apparently normal liver?

Dr. A. X. Rossien (*Kew Gardens, N. Y.*):—Can you tell us from your experience how frequently you have found, when you did the biopsy puncture, that you got normal findings instead of the pathological findings that you expected simply because the biopsy puncture must be done blindly unless it is done with the aid of a peritonescope to guide you?

Dr. I. R. Jankelson (*Boston, Mass.*):—I am the only one who has questions to answer.

A question was asked by Dr. Cunha about a man who was drinking four or six quarts of liquor a day for a good many years and never had had any cirrhosis. The only explanation I have for that is that he probably ate well. He was financially able, as Dr. Cunha mentioned besides the $40.00 a day for liquor, to get average food and that is the reason he did not get cirrhosis of the liver.

As to Dr. Rossien's question, it is no doubt true that liver biopsy does not completely exclude cirrhosis of the liver. You may strike a normal area where disease is not present. That is why I said in my paper that a diagnosis of a normal liver can be made with some reservation on the basis of a liver puncture biopsy. When, however, the disease is diffused as in cirrhosis of the liver you get evidence of the disease. You do not necessarily strike the most involved area. You might get evidence of a mild involvement. In other areas of the liver, there might be a much greater involvement or vice versa. But you do get in about 90 per cent of the cases where you do a liver needle biopsy sufficient evidence to say that there is a diffused involvement of the livr in cirrhosis of the liver.

Dr. Rossien:—Suppose it is not diffused?

Dr. Jankelson:—Well, usually it is diffused. You are going to get areas of cirrhosis and you know it is there.

AMEBIASIS IN TUBERCULOSIS PATIENTS*†‡

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Introduction

Although numerous investigations of the incidence of amebiasis have been made none has come to our attention in which the study was directed toward a group of patients having tuberculosis. The coexistence of these two diseases offers an opportunity to observe not only their reciprocal influence but also the effect of antituberculosis drugs upon the protozoan infection.

This report is limited to a consideration of amebiasis as observed among patients in the Triboro Hospital, a municipal tuberculosis institution of greater New York City. Patients usually remain for longer periods of time in tuberculosis than in general hospitals and, consequently, the opportunity for long-term study is thereby afforded. For example, the average patient's residence during 1952 was 165 days at the Triboro Hospital and 18.5 days at its sister institution, the Queens General Hospital, or a ratio of 8.9:1 days of hospitalization. Being isolated from the general population and living under better sanitary supervision, the sources for parasitic infection are markedly reduced.

The combined aforementioned factors presented an excellent opportunity for this study.

Methods

Nonambulatory and surgical ward patients were not used as subjects for this investigation. The medical wards were chosen at random, while the patients were selected according to the alphabetical arrangement of their names in their respective ward. With a few exceptions the patients had pulmonary tuberculosis of varying degrees of severity. The exceptions were patients who were under observation for chronic pulmonary disease but the diagnoses of the types of their diseases were not fully established.

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This study was begun in May 1952 and continued for a period of ten months. A total of 264 patients was examined which consisted of 160 (60.6 per cent) males and 104 (39.4 per cent) females. Although these patients were predominantly from the United States, many were of recent foreign residence.

On the basis of the average daily hospital census of 607, the total number of patients that were under investigation in this study was 43.5 per cent of the average patient population.

Examination of the stool was conducted according to the following routines: (A) One casual ("cold") specimen was collected by the patient directly in a paper cup on the day before examination. This specimen was concentrated by the zinc sulfate centrifugal flotation method[1] and examined after treatment with D'Antoni's iodine stain[2]. Other specialized concentration methods used on this

TABLE I

EXAMINATIONS AND TECHNICS USED IN THE INVESTIGATION

Total number of patients examined		264
Type of stool specimen	Technic	
Cold	Zinc sulphate concentration	278
Warm unsatisfactory	Direct, saline dilution	99
Warm satisfactory	Direct, saline dilution	245
Cold	Gravity sedimentation	13
Cold	Acid-ether concentration	3
Warm	Culture	2
Total number of stool examinations		640*
Average examinations per patient		2.4

*Does not include follow-up examinations

casual specimen were: (a) A gravity sedimentation concentrate[3] was prepared and examined when indicated because of the patient's possible exposure to *Schistosoma mansoni* or *japonicum*. (b) Specimens of patients who had been in the Far East were additionally concentrated, using an acid-ether technic, and examined.

(B) on the morning of examination the patient was given a magnesium sulfate purge following which at least one satisfactory stool was collected directly in a paper cup. A semisolid or liquid postcathartic specimen was considered a "satisfactory" stool. This specimen was examined on a warm slide with saline dilution within 15 minutes after collection. The purged specimens of most of the patients with amebiasis were preserved on slides with polyvinyl alcohol fixative[4] for later staining with iron-hematoxylin[5].

Exclusive of follow-up stool studies a total of 640 examinations were carried out. This is an average of 2.4 examinations per patient. Table I summarizes the types of studies carried out.

We planned to examine one casual and at least one satisfactory postcathartic specimen from each patient under observation. We considered these as the minimum number of specimens that could be required to conduct this type of investigation. Thirty-eight patients, who had been in areas where amebiasis is highly endemic, had negative stools obtained as mentioned above. We obtained additional purged specimens from them. The aforementioned routine specimens were considered adequate for the remaining 226 patients.

Data Obtained

In this series of 264 patients 33 (12.5 per cent) were found to have amebae in their feces. Only 9 (3.4 per cent) of all of the patients, however, had the pathogenic organism, *Endameba histolytica.* Hence, it will be noted that in this series there was a lower incidence of amebiasis than usually reported in the literature. It was interesting to observe that 5 of our 9 cases of amebiasis were infected by a small race of *E. histolytica.* A subsequent report will be made relative to this finding in our investigation. The incidence of each of the different species of amebae that were observed is recorded in Table II. Of these different species 27 per cent were *E. histolytica.*

TABLE II

Amebae Found

Endameba histolytica	9	(3.4%)
Endameba coli	8	(3.0%)
Endolimax nana	10	(3.8%)
Iodameba butschlii	3	(1.1%)
Dientameba fragilis	3	(1.1%)

Discussion

There are reports of surveys in which the incidence of amebiasis has been found to be less than five per cent[6]. It is noteworthy that in almost all such surveys the data were derived from single stool examinations. In order to disclose the real incidence, however, a sufficient number of examinations must be made and the examiner must be technically expert. The preponderance of informed opinion indicates an actual overall incidence of amebiasis in this country of 10 per cent or more[6,7].

Lincicome and his coworkers were of the opinion[8] that a single stool examination will disclose between 30 to 40 per cent of the actual total number of cases of amebiasis. They believe that examination of 3 or more fecal specimens will almost double the number of cases disclosed. Craig[6] stated that an average of 1.6 examinations per patient will reveal less than one-half of the actual number of amebic infections. On the other hand, Shookhoff[9], emphasizing the value of examining fresh-purged stool, found that among 282 amebiasis patients 208 (%) of these cases presented *E. histolytica* in the first satisfactory purged specimen.

In the series herein reported we might have disclosed a larger number of cases of amebiasis if 2 or 3 purged specimens were examined from each patient. Nevertheless, it is our impression that relatively few cases of amebiasis remained undiagnosed since a minimum of 1 cold and 2 purged specimens were examined from all of the patients who were geographically, clinically or microscopically under suspicion. The rather low incidence (3.4 per cent) in our series requires an explanation. The fact that an average of 2.4 specimens per patient were examined and that a large number of the patients had been in areas where amebiasis is highly endemic tends to justify our impression that this observed incidence is significantly low.

That this low infection rate may be related to the pulmonary disease or to the hospitalization itself with its attendant isolation and enforced physical rest are speculative hypotheses. Another possible explanation is the increasing use of aureomycin and terramycin. These drugs undoubtedly cure a number of silent amebic infections without the knowledge of either patient or physician. In the

TABLE III

GEOGRAPHIC DISTRIBUTION OF AMEBIASIS

Area	Number of patients	Patients with amebiasis	Incidence by area
Northern United States and Alaska	97	2	2.1%
Southern United States	71	3	4.2%
Western Europe and Balkans	65	3	4.6%
Central America	19	1	5.3%
Caribbean area	25	0	0.0%
Near East, India, Far East	11	0	0.0%

majority of such cases, however, in our series it is doubtful whether the amount of antibiotic prescribed was adequate to cure permanently the protozoan infection[10,11]. Although we do not have reliable information as to the frequency with which these drugs had been given to the patients under study, it is, nevertheless, possible that such cryptic cures have occurred.

A more probable explanation for the low incidence is that it is the end result of administration of antituberculosis drugs given to these patients in large amounts over long periods of time. Most of the patients in our series had been given isonicotinic acid hydrazide (isoniazid), streptomycin and para-aminosalicylic acid (PAS).

Isoniazid was given in doses of 5 to 7 milligrams per kilogram of body weight for periods of 6 to 12 months. This drug has sharply limited antibacterial activity. We are informed that it is not active against *E. histolytica* in rats[12]. Our findings reveal (Table IV) that the incidence of amebiasis among isoniazid-treated patients is 4.5 per cent as compared with a rate of 3.4 per cent among those who had not received that drug, both groups having been given streptomycin-PAS

as well. There is no significant difference between these rates so that there is no evidence that isoniazid had amebacidal activity.

PAS was usually given to almost all of the patients in doses of 12 grams daily, concurrently with streptomycin. Consequently no analysis can be made which would disclose its effect as an amebacide separate from the amebacidal effect of streptomycin.

Streptomycin, on the other hand, has some activity against a variety of lower biologic forms, including some of the constituents of the bowel flora with which *E. histolytica* lives symbiotically. This antibiotic is irregularly and temporarily bactericidal against coliform bacteria in the human bowel[13]. It is a moderately active amebacide in rats[14]. There are few reports of its effectiveness in human amebiasis. De Paula[15] found in 1950 that 6 cases which failed to respond to standard amebacides "showed improvement" with "sulfasuxidine or antibiotics, notably streptomycin given in doses of 1 gram daily for 15-20 days". Eldson-Dew

TABLE IV

ANTITUBERCULOSIS DRUGS AND AMEBIASIS

Drug	Number of cases*	Positive for E. histolytica	Rate
None	8	0	0%
Isoniazid	1	0	0%
Streptomycin-PAS	148	5	3.4%
Streptomycin-PAS and isoniazid	89	4	4.5%

*These consist of 246 cases from whom an adequate history of therapy could be obtained.

et al[16] treated 17 cases of amebiasis with streptomycin in doses of 2.0 grams daily for 10 days. Short term follow-up studies done 17 days after completion of the treatment revealed 70 per cent failures. It is likely that other workers used streptomycin for the definitive treatment of amebiasis with indifferent results and therefore refrained from publishing their findings. It should be noted, however that this drug given to the patients in our series was usually continued for 6 to 12 months at a dosage level of 3.0 grams per week. This relatively long duration of treatment could have been a factor in the more pronounced amebastatic effect noted in our findings.

If one were to assume the expected incidence of amebiasis in a study of this kind to be 10 per cent (a rate that would be considered conservative by many experienced parasitologists), the incidence actually observed (3.4 per cent) in this series of cases is but one-third of that anticipated. Inasmuch as the cure rate of conventional therapy is 80 per cent to 90 per cent, streptomycin-PAS

cannot be considered a reliable amebacide even though, as used in these cases, it can be expected to lower the observed incidence of the disease by two-thirds.

A comparison of the incidence of amebiasis in the group that had received streptomycin-PAS with the group that had not would be desirable. There were only 8 patients, however, who had not received these drugs. This is too small a control group to be of value in assaying the effect of these drugs.

The observations made in the cases of 2 patients who had amebiasis and from whom it was decided to withhold specific treatment for the protozoan disease are significant. These patients were being treated with streptomycin-PAS at the time. In one of them, examination of casual and purged specimens done after 2 weeks of treatment with the antituberculosis drugs revealed no amebae. In a second case similar follow-up after 11 days of treatment with streptomycin-PAS revealed a very small number of trophozoites which were non-motile. It therefore should be borne in mind that negative examinations for amebiasis

TABLE V

Comparison of Symptoms Due to Amebiasis and to PAS

Case	Symptoms attributable to amebiasis	Symptoms attributable to PAS
FB	Diarrhea, abdominal pain, "gas"	none
EC	none	Diarrhea, nausea
RD	Diarrhea	none
AH	Nausea, vomiting, diarrhea, pain	none
LH	none	Diarrhea
EK	Constipation, abdom. pain, fatigue	none
JM	Abdominal pain	none
PM	none	Abdominal pain, diarrhea
HN	none	none

conducted at the time streptomycin-PAS is being used may give a false sense of security since these drugs may temporarily mask the protozoan infestation.

These observations lead us to regard streptomycin-PAS as an inefficient amebacide with an amebastatic effect similar to that of the sulfonamides or of penicillin.

Table V summarizes the symptoms of the patients with amebiasis. It is apparent that they may simulate those due to PAS toxicity. Indeed the parallel is close enough to make one cautious against assuming that gastrointestinal symptoms in PAS-treated patients are necessarily drug-induced or that abdominal symptoms in a patient with pulmonary tuberculosis are necessarily indicative of gastrointestinal tuberculosis[17].

All of the cases of amebiasis were of mild degree and unrelated to the severity of the tuberculosis process. No improvement of the tuberculosis could be ascribed

definitely to the cure of the parasitic infection. Amebic hepatitis was not observed. Ameboma is uncommon and was not seen in this group. This complication of amebiasis can be of special interest since it may be confused with intestinal tuberculosis[18].

Treatment of the amebic infection was carried out in 6 of the 9 cases. They were given Carbarsone® in the usual doses: 250 milligrams three times daily for 10 days. No undesirable side-effects were noted in this small group whether the drug was given alone or concurrently with streptomycin, PAS, or isoniazid. In all cases in which symptoms due to the parasitic disease had been present the patients noted marked improvement, and 2 stated that they felt better than they had "in years".

Follow-up examinations of the stool were possible in 4 of the 6 treated cases. Table VI, summarizing these data, reveals fairly satisfactory intervals elapsing between treatment and follow-up.

The geographic distribution of amebiasis showed the expected higher incidence in the southern United States, but the failure to find amebiasis in the

TABLE VI

FOLLOW-UP EXAMINATIONS

Case	Elapsed time from treatment to follow-up study	Findings on follow-up study	Treatment
FB	4 months	negative	Carbarsone
RD	3 "	"	"
AH	6 "	"	"
JM	8 "	"	"

group of 36 patients originating in the Caribbean area, the Near East and the Far East is unexplained except possibly on the basis of the small size of the group.

SUMMARY

1. Examinations for parasites conducted on 264 patients in a tuberculosis hospital in which 2.4 stool examinations per patient were carried out revealed 9 cases (3.4 per cent) of amebiasis.

2. Evidence is presented suggesting that the incidence of amebiasis was reduced as the result of prolonged treatment with streptomycin-PAS.

3. Streptomycin-PAS had little or no value as a definitive amebacide.

4. Carbarsone®, given to 6 patients, was an effective amebacide, and was non-toxic either used alone or concurrently with streptomycin, PAS, and isoniazid.

5. Isoniazid, as used in the treatment of tuberculosis, was inactive against *E. histolytica* in the group investigated.

6. Amebiasis may produce symptoms closely simulating the side-effects of PAS.

7. There were no cases of amebiasis of severity sufficient to alter the course of the tuberculous infection, and the presence of tuberculosis had no apparent effect on the protozoan disease.

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TRUE INTRAHEPATIC LITHIASIS

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Liver stones are exceptional observations. Before the advent of the roentgen era, they were exclusively autopsy findings with the exception of a few cases in which they were detected incidentally during operation. With the aid of the x-ray, intrahepatic stones containing calcium are amenable to preoperative or *intra-vitam* diagnosis. The number of cases of intrahepatic stones diagnosed by x-ray is exceedingly small. The case presented here is the third in a row in the author's series, diagnosed by roentgen demonstration.

The fact that the writer was able to diagnose three cases from his private practice in the course of less than ten years, when the entire literature on this subject could hardly muster even one or two hundred during half a century, seems to warrant the publication of this case.

Case Report

E. M., 43, female, married, first seen April 15, 1944. At that time the complaint referred to was lower backaches during the previous 5 years. A tremendous fibromyoma of the uterus, larger than a man's head, was found. This was undiagnosed heretofore. Operative removal (Dr. A. Stein, Lenox Hill Hospital). Part of the tumor was intraligamentous and there were adhesions all around. After the operation a secondary microcytic anemia with a 50 per cent hemoglobin developed, which yielded to treatment. Physical examination was otherwise negative. There were external hemorrhoids and a rectal fissure present, which occasionally caused some distress. The patient, being highly emotional, kept complaining about dizziness, headaches, colds, backaches, constipation, etc.

In recent months the patient complained of some pain in the right side of the lower back and also in the right hypochondriac region. These, as well as other complaints in the past ten years, were of mild nature, easily yielding to medical management. She never suffered from any serious or severe pain or painful attack, nor was she incapacitated even for a day; at no time did she have icterus or other signs or symptoms referable to the liver. Patient enjoyed good health throughout these years and she was always able to perform her daily work as a housewife. She put on about twenty more pounds to her overweight, and if she had any problem, this was it.

In August 1945, during a routine gastrointestinal x-ray examination, clusters of stone shadows were noted and diagnosed within the boundary of the liver. The gallbladder appeared normal and cholelithiasis was easily ruled out. In April 1953, re-examination was made and at that time during the x-ray check-up a retrograde urography was undertaken. The cluster of stones showed the same

type of arrangement and extent, as were noted in 1945, with the difference that the individual stones had increased in size. The gallbladder, as visualized by the Graham-Cole method, using telepaque, was of normal size, shape, configuration and dye concentration; it reduced its size upon administration of fatty meal. The cluster of stones were lateral to the gallbladder. The catheter in the right ureter led to the immediate vicinity of the stone conglomerate. Pyelogram proved to be normal. The cluster of stones visualized were outside of this domain (retrograde urography was performed by Dr. Monroe Greenberger). The gallbladder and the right kidney-pelvis were accordingly ruled out as the organs possibly harboring the stones, with the inference that the stones within the

Fig. 1a Fig. 1b

Fig. 1—Intrahepatic stones, 1954. (a) posterior-anterior view. (b) lateral view.

boundary of the liver must consequently be contained in the liver proper, respectively in its intrahepatic ducts. These were considered as the site of their origin.

Of course, in this, as well as in the cases previously published final diagnosis was established only after the proper exclusion in the participation of stone formation of all the extrahepatic biliary structures (gallbladder, cystic, hepatic and common ducts), and the exclusion of all possible causes which might produce similar or comparable x-ray shadows, such as stones in the right kidney, pelvis, calcified glands, calcification of the cartilages of the ribs, drugs, foreign

bodies, remnants of the gallbladder dye, barium retention in the diverticula of the colon, calcium content in scars, tumors, cysts (dermoid, teratoma, ecchinococcus, etc.).

Classification

In my opinion a clear classification of the liver stones can be accomplished on the following basis:

1. Intrahepatic stones designate the presence of stones in the liver, regardless of their origin or etiology. In this condition some of the stones, originally

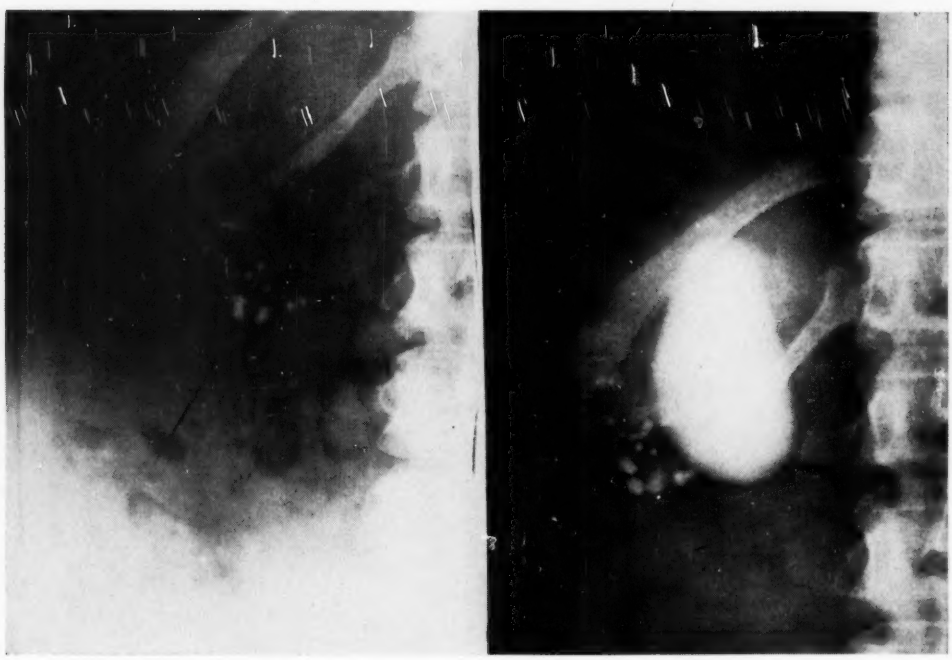

Fig. 2a Fig. 2b

Fig. 2—Intrahepatic stones, 1953. (a) posterior-anterior view. (b) cholecystogram.

formed in the gallbladder, are moved to the adjoining and contiguous extrahepatic ducts, the cystic, the common and the hepatic. From the hepatic ducts they may, under certain favorable conditions, reach the contiguous smaller ducts and finally the finest biliary radicles. The majority of all the reports published belongs to this group.

2. Intrahepatic lithiasis designates the intrahepatic biliary passages as the site of stone formation. The intrahepatic biliary passages are both, the site of formation and location as well. Here, the gallbladder and the extrahepatic ducts do not partake in identical or even in similar stone formation, although they are

diseased, exhibiting some unrelated pathology. This pathology and, if stones are present, their character and chemistry, are not identical with the ones found in the intrahepatic passages. Our second case, reported in 1936, belongs to this group. Here, in addition to the intrahepatic stones, there was also found in the gallbladder, a solitary, huge cholesterol stone, an incidental finding, detected at operation. The intrahepatic stones consisted of numerous, small, calcium containing concrements appearing in a cluster; while the cholesterol stone did not contain calcium, was not opaque to x-ray and was solitary. The latter developed independently and was not related to the intrahepatic stones. Only a small percentage of the reported cases belongs to this group.

3. True intrahepatic lithiasis could be applied to a third group of cases, in which intrahepatic lithiasis is the only pathology noted. Stones are formed and located in the intrahepatic biliary passages, without any participation of the extrahepatic structures in any stone formation. Gallbladder and all the extrahepatic ducts are free from any pathology. These cases are extremely rare. Only a few cases reported in the literature could be classified in this category. The case presented here, as well as the first case, reported by us in 1936 belong to this group.

Rufanov in 1936 likewise made a similar classification in three groups, on a somewhat similar though not identical basis.

Incidence

Large autopsy materials were subjected to careful study to determine the incidence of the intrahepatic stones, a short resumé being: Courvoisier (1903) found in a material of 16,065, cholelithiasis 1,714 times, liver stones only once; Hesse (1911) found in 17,002 cases cholelithiasis 278 times, liver stones only once; Beer (1904) found in 250 dissected livers (of patients who died of cholelithiasis), liver stones six times; Miyake in Japan (1913) established a record of twenty liver stones in 8,406 patients among 257 cholelithiasis cases. Courvoisier collected 50 cases from the literature in 1891, Beer 150 in 1904, Rufanov found only 62 in 1936. Feldman reports a necropsy incidence of 1 to 25,073.

Discussion

The literature on liver stones is exceedingly meager. The published material refers mostly to cases with intrahepatic stones, with primary participation of the gallbladder in the stone formation and location as well. The extrahepatic ducts may or may not be involved. Very rarely has the gallbladder been found free, when the large extrahepatic ducts contained stones. There are scarcely any cases on record of true intrahepatic lithiasis. Considering this scarcity of published reports, it is all the more astounding that I have been able to diagnose three cases in my own practice of real intrahepatic lithiasis.

Even if the incidence were as rare as 1 to 25,000, with autopsy material covering millions of cases in many countries, the number of published cases

remains exceedingly small. Practically all the cases known are incidental autopsy findings with a few operative observations. I did not come across any published report, outside of my own, in which diagnosis was made, *intra-vitam*, by x-ray visualization of the stones.

Bockus in his book on "Gastroenterology" spends only a few lines on the topic of intrahepatic stones, by stating, that: "intrahepatic stones are seen occasionally but they are rare". Furthermore: "the number of stones which may be found is variable; in about two thirds of the cases a single stone is found, and even in those where calculi are multiple large numbers are exceptional" (Walters and Snell).

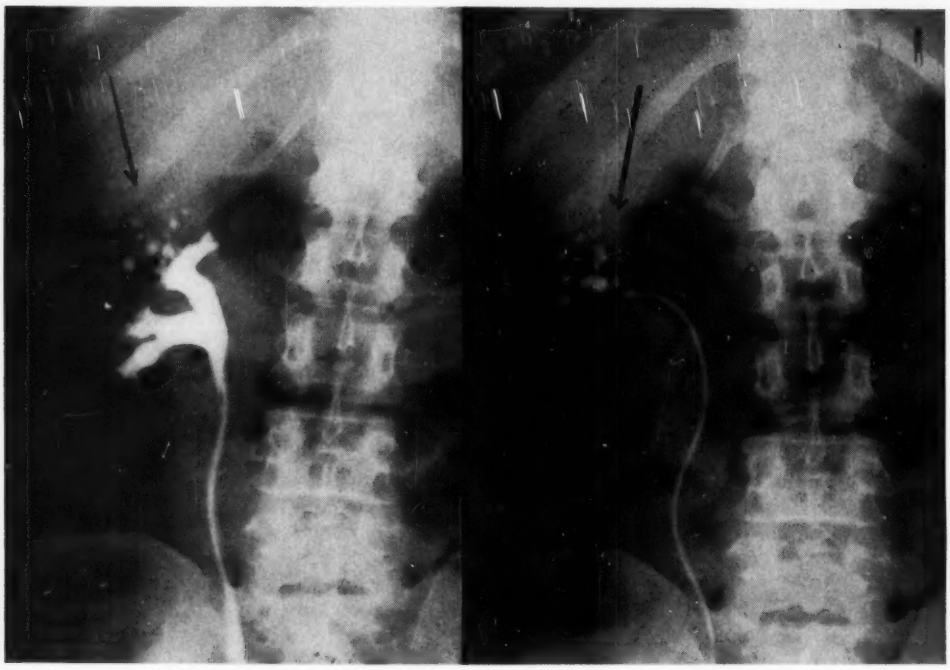

Fig. 3a Fig. 3b

Fig. 3—Intrahepatic stones, 1953. (a) pyelogram. (b) right ureter catheter *in situ*.

Feldman gives a little more space for its detailed description, even quoting data from the literature. Portis in his recent book fails to mention the intrahepatic stones. Nor is there any reference in the other standard and excellent books by Assmann, Carman, S. Weiss, Meyer, Stierlin-Chaoul, Holmes and Ruggles, Lyon, or Buckstein.

Bockus mentions migration, passage and dislodgement by operative manipulation in explaining the removal of stones from one location to another. As a common rule the gallbladder is the site of stone production. It harbors stones,

often in large numbers. They may, by their increase in size and number secondarily invade and jam *per viam necessitatis* the adjoining passages. First, the extrahepatic ducts are involved, but later, when still more room is needed for further expansion, stones also will be forced into, and may attain access in the smaller intrahepatic ducts. As against this mechanism stones may also migrate in the opposite direction. Graham and Cole state: "that stones found in the cystic or common duct may have their way there from the gallbladder or the intrahepatic ducts". . . . "small stones formed in the intrahepatic ducts may find their way into the gallbladder by reason of the normal ebb and flow of bile and act as nuclei for the formation of larger gallstones". Of course, this latter possibility, if it ever were present, must be very exceptional, indeed, if for no other reason than the rarity of the occurrence of a primary intrahepatic stone.

The majority of case reports belong to the first group, i.e. the group of "intrahepatic stones" of our nomenclature. The cases of Beer, together with those of the German authors quoted by him (Naunyn, Kehr, Riedel, Czerny, etc.) as well as those of Koster and Gerber, Lewisohn, etc., all belong to this group.

Choledocholithiasis (Danzis), and liver stones (Leopold) in the extremely rare cases of congenitally absent gallbladder deserve special interest, as they point to the fact that the gallbladder is not necessarily the only place where stones are formed.

Presence of stones in the extra- or intrahepatic passages or both, with normal gallbladder serves to prove the same. Normal gallbladder was found in the case of Judd and Burden, in which surgery was performed for extrahepatic ductal lithiasis, and incidentally also intrahepatic stones were detected, or in the case of Vachel and Burden (quoted by Judd and Burden), in which in the presence of over 100 stones in the extrahepatic ducts, the intrahepatic passages contained 520 small stones.

In Lenhartz's case (quoted by Rufanov) intrahepatic stones were found in absence of any pathology in the gallbladder.

A few data referring to the clinical aspects of this disease can be better evaluated today than at the time when they were presented.

Murchison in 1885 stated that no intrahepatic stones were found in presence of normally functioning patent choledochus. Rufanov observed that the liver and gallbladder are enlarged and the majority of cases of intrahepatic stones are accompanied by jaundice. Judd and Burden found that: "in most cases of intrahepatic stones reported patients were acutely ill, gravely ill, often jaundiced". Rolleston remarks that these intrahepatic calculi almost necessarily set up jaundice and pericholangitis. In Murchison's description the symptomatology is obscure, jaundice is absent and pain and colic may occur, etc.

All these observations and descriptions, in my opinion, have one thing in common: they refer to cases of intrahepatic stones, in which the primary disease

is a severe and complicated cholelithiasis, and do not represent the symptomatology of the intrahepatic stones. The occurrence of some of the stones in some of the intrahepatic passages, may represent one of these complications, or it may be an incidental finding, which is not necessarily responsible for any or all the signs and symptoms referred to. Intrahepatic stones were not the primary or sole disease and the above descriptions were not, per se, indicative of liver stones, rather they were part and parcel of a chronic and neglected, complicated cholelithiasis. If stones were in the cystic duct, pain prevailed, if they were in the choledochus, painful attacks, jaundice, chills, fever and acute illness were the symptoms. Further complications involved cholangitis, abscess formation and other consequences of a grave illness.

None of the aforementioned serious symptoms or signs were present in any of my three cases referred to. In the first two cases there were some symptoms, such as occasional pain and vomiting, which possibly might have been correlated to the stones in the liver. There were no definite signs or symptoms in the case presented here, referable to the lithiasis.

That would answer the question of symptomatology. There are no signs or symptoms which are necessarily caused by the presence of stones in the liver. They may develop and they may vary according to the size, number, location and surface of the stones, or extent of the lithiatic process. In cases with participation of wide areas stones may obstruct the biliary passages, causing jaundice, decubitus, bleeding, ulcer, abscess, cholangitis, etc. But none is a prerequisite. None is a symptom or sign per se.

Feldman states, that: "hepatolithiasis is rarely diagnosed by the roentgen examination because they are composed chiefly of bile salts and cholesterin which are nonradiable". In all three cases of mine the opposite held true. They all contained enough calcium to be clearly visualized and in all three cases *intra-vitam* and preoperative x-ray diagnosis has been established. Of course it remains questionable as to how many more cases of the same material remained undiagnosed by failure of x-ray visualization on account of their lacking calcium content. My observations are not corroboratory of the scanty notes of Bockus on this subject. As for the calcium content of the liver stones, due to the fact that in most cases the stones located in the liver originate in the gallbladder, it is fair to assume that their opacity and calcium content cannot greatly differ from that of the gallstones.

Summary

A case of true intrahepatic lithiasis is reported. Clusters of stones were diagnosed by x-ray, with a localization in the liver itself. Gallbladder and the extrahepatic ducts were clinically as well as also roentgenologically free from stones. The case has been under observation for over eight years. There were no clinical signs or symptoms attributed to the presence of stones.

True intrahepatic lithiasis is extremely rare or rarely diagnosed. Few, if any case reports are published in the literature. This case is the third in the author's series.

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President's Message

With this issue we initiate a change in our publication which now becomes THE AMERICAN JOURNAL OF GASTROENTEROLOGY. Change in itself is not important, but when the change represents progress and advancement it expresses vitality and a desire to meet the challenge of our present day.

We hope through our journal to advance the cause of Gastroenterology. At present we find very few medical schools who have a separate department of Gastroenterology. We hope to encourage the establishment of departments of Gastroenterology so that both undergraduates and postgraduate courses in Gastroenterology will be available to those who wish to specialize in this field.

We also hope to encourage the establishment of departments of Gastroenterology in hospitals. As a result of a survey conducted by the National Gastroenterological Association some time ago, we were amazed to find so few hospitals with separate departments in this field.

Finally we hope to stimulate interest in Gastroenterology so that more of our young medical graduates will find it worthwhile to prepare themselves in this field and take the Board examinations certifying that they are qualified to practice Gastroenterology.

All these aspirations are voiced in our new name and as our organization grows we hope to see our AMERICAN JOURNAL OF GASTROENTEROLOGY grow in quality and ever increasing usefulness.

Sigurd W. Johnsen

EDITORIAL

The American Journal of Gastroenterology

With this issue, the official publication of the National Gastroenterological Association proudly assumes the title, The American Journal of Gastroenterology which has been incorporated as the sub-title of The Review of Gastroenterology since the July-August 1942 issue.

The first issue of the old American Journal of Gastroenterology was published in 1911 under the auspices of the American Hospital for Diseases of the Stomach in Philadelphia. The first editors were the late Dr. Louis Brinton and our own Honorary President, Dr. Anthony Bassler. In 1912, the journal appeared as an independent publication. In 1916 it was merged with "The Proctologist" and was published in St. Louis as "The Proctologist and Gastroenterologist". The editor and publisher of the merged journal was Rollin H. Barnes and Drs. Brinton and Bassler were the editors of the gastroenterology section. The final issue of this journal appeared in December 1916 and to this date, no subsequent issues have been published.

Through the efforts of our historian, Dr. Hyman I. Goldstein, the history of The American Journal of Gastroenterology was traced back to its initial issue[1,2]. In January of 1942, the Board of Managers of the American Hospital of Diseases of the Stomach of Philadelphia, through its president, Dr. W. Wilson McNeary, authorized The Review of Gastroenterology to use the title of their old and defunct publication. On behalf of the National Gastroenterological Association, we extend to them our sincere thanks and gratitude for this kind permission.

Dr. Anthony Bassler, the only living person previously associated with the former American Journal of Gastroenterology, has also given us his consent to the use of this title.

With this proud heritage, The American Journal of Gastroenterology takes its place as one of the foremost and oldest journals in the field. We proudly look back upon our record as The Review of Gastroenterology and look forward to the years ahead as The American Journal of Gastroenterology.

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REGIONAL ACTIVITIES

Central Region

The first regional meeting of the National Gastrcenterological Association since the regions were created at the annual meeting of the Association in 1953, will be held in Milwaukee, Wisc. The one day session will take place at the Schroeder Hotel on Sunday afternoon, 28 March 1954. The local committees appointed for the regional meeting are:

Program Committee:—Dr. Michael W. Shutkin, chairman, Dr. M. C. F. Lindert and Dr. Albert G. Schutte.

Publicity Committee:—Dr. Jack Levin, chairman and Dr. Cornelius J. Corcoran.

Housing, Arrangements and Luncheon Committee:—Dr. Leonard J. Schwade, chairman, Dr. M. E. Gabor and Dr. Walter J. Schacht.

Program and Registration Committee:—Dr. Isadore I. Cash, chairman.

Projection Apparatus Committee:—Dr. Robert T. McCarthy, chairman.

Ladies Committee:—Mrs. Joseph Shaiken, chairman, Mrs. Michael W. Shutkin, Mrs. Walter J. Schacht and Mrs. Jack Levin.

The program will appear in the February 1954 issue of The American Journal of Gastroenterology.

Members of the medical profession are cordially invited to attend.

NEWS NOTES

Executive Committee Meetings

A meeting of the Executive Committee of the National Gastroenterological Association was held on 12 August 1953 in New York City. Routine administrative matters were discussed and properly disposed of.

In the absence of the Secretary-General, Dr. Roy Upham, who was in Europe, Dr. William C. Jacobson reported that the New York Chapter had tendered a dinner in honor of Dr. Upham on 21 May 1953 and that the Boston Chapter had held a regular meeting on 27 April.

Dr. Elihu Katz, Treasurer, presented the financial statement and advised that the new system of accounting and bookkeeping suggested by the accountant had been put into effect.

The Los Angeles and New York Chapters presented for ratification the applications of the following, which applications were approved by them and accepted by the Executive Committee. Dr. Robert B. Hope, Los Angeles, Calif.; Dr. Nathan Brodie, Brooklyn, N. Y.; Dr. Merton Leopold Brown, New York, N. Y.; Dr. Samuel Kalfus, New York, N. Y.; Dr. Ernest Lehman, Brooklyn, N.Y.; Dr. Roman H. Perkul, New York, N. Y.; Dr. Chester Sidney Svigals, New York, N. Y. and Dr. Berthold Weingarten, New York, N. Y.

The applications of the following were accepted for membership at large in the National Gastroenterological Association. Dr. Louis Kenneth Beasley, St. Louis, Mo.; Dr. Max Caplan, Meriden, Conn.; Dr. D. C. Rodgers, Chicago, Ill.; Dr. Bernard Farfel, Houston, Texas; Dr. Robert J. Gross, Newark, N. J.; Dr. Waldemar B. Hartmann, Mt. Clemens, Mich.

Upon presentation of the necessary qualifications, the following were advanced as indicated: Dr. Lester Crismon, Aruba, N. W. I., Fellow; Dr. Richard Edgar Dunkley, Washington, D. C., Associate Fellow; Dr. Charles H. Helman, Bronx, N. Y., Associate Fellow; Dr. S. William Kalb, Newark, N. J., Fellow; Dr. Jordan Propatoridis, Athens, Greece, Fellow; Dr. Arthur James Statman, Newark, N. J., Associate Fellow and Dr. Jerome Weiss, New York, N. Y., Fellow.

Dr. Samuel Weiss, Editor, reported that a readership survey conducted amongst the readers of The Review of Gastroenterology indicated that the publication was among the first two journals in the field. The Review of Gastroenterology received one more vote for first place than did the journal of second choice.

He further reported that the change in format and appearance and the new cover which were introduced in May had met with approval and would be continued.

Reports of other committees were presented and accepted.

At the suggestion of Dr. C. J. Tidmarsh, the President, Dr. Felix Cunha appointed an exploratory committee of three, consisting of Dr. C. J. Tidmarsh, chairman, Dr. Sigurd W. Johnsen and Dr. Anthony Bassler. This committee was to meet with a similar committee to be appointed by the American Gastroenterological Association for discussing mutual problems existing between the two organizations.

The next meting of the Executive Committee was the annual meeting held at The Biltmore Hotel in Los Angeles, Calif. on Sunday, 11 October 1953.

Dr. Roy Upham, Secretary-General, reported on his trip to Europe and the contacts which he had made on behalf of the Association. He further reported on the forthcoming IVth European and Mediterranean Congress of National Gastroenterological Associations which was to be under the Presidency of Dr. René Gutmann. The National Gastroenterological Association was to be officially represented at this Congress by Dr. Upham and a committee of three.

The Treasurer, Dr. Elihu Katz, reported on the financial status of the Association and presented an estimated budget for the year 1954, which was adopted as presented.

The applications of the following were accepted for membership at large in the National Gastroenterological Association. Dr. Victor H. Fink, Chicago, Ill.; Dr. Basile Karageorgis, Athens, Greece; Dr. Sylvan Strong Scholpp, Phoenix, Ariz.; Dr. Bernard Stern, Miami Beach, Fla. and Dr. Thomas Wilensky, Lansing, Mich.

Upon presentation of the necessary qualifications, the following were advanced as indicated: Dr. Samuel S. Gilbert, Brooklyn, N. Y., Associate Fellow; Dr. Stanley Stark, Brooklyn, N. Y., Associate Fellow; Dr. Vikit Viranuvatti, Bangkok, Thailand, Associate Fellow and Dr. Sidney Lechner, Bronx, N. Y., Fellow.

The names of Drs. William Reid Morrison, Boston, Mass.; Richard Bauer, New York, N. Y.; Jacques Caroli, Paris, France and P. Mallet-Guy, Lyons, France, were recommended to the National Council for election as Honorary Fellows.

Dr. Frank A. Cummings, chairman of the Membership Committee, reported a total of 783 Members in the Association, consisting of 17 Honorary Fellows; 19 Life Fellows; 279 Fellows; 123 Associate Fellows and 345 Members.

Dr. Samuel Weiss, Editor, of THE REVIEW OF GASTROENTEROLOGY reported for the Editorial and Publications Committee and announced the appointment of Dr. Joseph R. Van Dyne of Forest Hills, New York, as chairman of the Abstract Committee for THE REVIEW OF GASTROENTEROLOGY. He further stated that $4,000.00 in surplus funds had been turned over to the Treasurer for the use of the Association.

Dr. Arthur A. Kirchner reported for the Program Committee and Dr. Lynn A. Ferguson reported for the Committee on Public Relations.

Annual Meeting of the National Council

The annual meeting of the National Council of the National Gastroenterological Association was held at The Biltmore Hotel in Los Angeles on Sunday, 11 October 1953.

The minutes of the Executive Committee meeting and the actions taken by the committee in the interim between Council meetings were unamimously approved.

The Council heard reports of the various committee chairmen.

The site of the 1958 Convention was discussed and the Executive Officer was directed to communicate with hotels in New Orleans, La., to obtain accommodations for 1958.

By unanimous vote, the following were elected to Honorary Fellowship in the National Gastroenterological Association. Dr. Rudolf Nissen, Basel, Switzerland; Dr. René Gutmann, Paris, France; Dr. Jacques Caroli, Paris, France; Dr. P. Mallet-Guy, Lyons, France; Dr. Richard Bauer, New York, N. Y. and Dr. William Reid Morrison, Boston, Mass.

Annual Meeting of the National Gastroenterological Association

The annual meeting of the National Gastroenterological Association was held at The Biltmore Hotel in Los Angeles, Calif., on Monday, 12 October 1953.

Dr. Felix Cunha, President, presided. The various committee chairmen gave their reports and the Treasurer, Dr. Elihu Katz, presented an audited statement for the year ending 31 December 1952.

The Secretary reported that no additional nominations for office had been received and upon motion duly made, seconded and carried, he was instructed to cast one vote for the slate presented by the Nominating Committee.

The Committee on Constitutional Revision submitted a series of amendments to the constitution and by-laws which radically changed the organization of the Association. These amendments were unanimously adopted.

It was announced that the dates for the next Convention were 25-30 October 1954 at the Hotel Shoreham in Washington, D. C.

Eighteenth Annual Convention

The Eighteenth Annual Convention of the National Gastroenterological Association which was held in Los Angeles, Calif., saw an attendance which equalled the registration at the previous Convention in New York City. The excellent scientific program arranged by the Program Committee with the cooperation of Dr. William C. Boeck and Dr. Lester M. Morrison was well received by those in attendance.

On Monday evening, the Fifth Annual Convocation took place and certificates of election and advancement were presented. The officers of the Association were present and heard an invocation delivered by Dr. Edgar Magnin of the Wilshire Blvd. Temple and a benediction by Dr. Theodore Palmquist of the Wilshire Methodist Church. Dr. Paul D. Foster, President of the Los Angeles County Medical Society, was the principal speaker and a certificate of Honorary Fellowship was given to Dr. Hyman I. Goldstein, historian of the National Gastroenterological Association.

Following the convocation, in accordance with the usual custom, the members and guests attended the President's reception sponsored by Winthrop-Stearns, Inc.

At the annual banquet on Tuesday evening, 13 October 1953, those assembled enjoyed an excellent dinner and listened to an address on "Molecular Medicine" delivered by Dr. Linus Pawling.

Dr. Sigurd W. Johnsen, incoming President, received the President's insignia from Dr. Felix Cunha, the outgoing President, who in turn was given a Past President's key by Dr. William W. Lermann.

Course in Postgraduate Gastroenterology

The Annual Course in Postgraduate Gastroenterology of the National Gastroenterological Association was given at The Biltmore Hotel and the College of Medical Evangelists in Los Angeles. Dr. Owen H. Wangensteen and Dr. I. Snapper again were the co-chairmen and the clinic was under the competent direction of Dr. Rudolf Schindler of the College of Medical Evangelists.

The American Academy of General Practice approved the Postgraduate Course for formal study credit for those of its members who attended.

The next Course in Postgraduate Gastroenterology will be given in Washington, D. C., immediately following the 19 Annual Convention and will again be under the direction of Dr. Wangensteen and Dr. Snapper.

Ladies Auxiliary

The Ladies Auxiliary, under the Presidency of Mrs. Felix Cunha, provided an interesting and varied program for those ladies who attended the Convention.

At a business meeting held on Monday afternoon, 12 October 1953, the following officers were elected. Mrs. Sigurd W. Johnsen, Montclair, N. J., President; Mrs. Lynn A. Ferguson, Grand Rapids, Mich., Vice-President; Mrs. Louis L. Perkel, Jersey City, N. J., Treasurer and Mrs. Elihu Katz, West Orange, N. J., Secretary.

A resolution adopting dues of $2.00 per year was approved and a letter was to be sent to the ladies, advising them of this action and asking for their cooperation and support.

A very competent committee of ladies from Los Angeles were present each day to register those who desired to participate in the auxiliary activities. These activities consisted of attending the convocation and the President's reception on Monday; a sight-seeing tour of a movie studio and lunch at the Farmer's Market and the annual banquet on Tuesday; a luncheon and floorshow at the Rendezvous Room at The Biltmore Hotel on Wednesday.

Plans for activities in Washington in 1954 were discussed.

Special Meeting of the National Council

A special meeting of the National Council of the National Gastroenterological Association was called by the President, Dr. Sigurd W. Johnsen, for Wednesday, 14 October 1953 at The Biltmore Hotel in Los Angeles.

Dr. Johnsen presented for approval the appointment of the following standing committees.

Program Committee:—Dr. Lynn A. Ferguson, Grand Rapids, Mich., chairman; Dr. James T. Nix, New Orleans, La.; Dr. Arthur A. Kirchner, Los Angeles, Calif.; Dr. C. Wilmer Wirts, Philadelphia, Pa.; Dr. Frank J. Borrelli, New York, N. Y.; ex-officio, Dr. Anthony Bassler, New York, N. Y. and Dr. Roy Upham, New York, N. Y.

Membership Committee:—Dr. Frank A. Cummings, Providence, R. I., chairman; Dr. Felix Cunha, San Francisco, Calif.; Dr. Bruce Lockwood, Detroit, Mich.; Dr. Harry M. Eberhard, Philadelphia, Pa.; Dr. I. R. Jankelson, Boston, Mass.; Dr. F. H. Voss, Phoenicia, N. Y.

Editorial and Publication Committee:—Dr. Samuel Weiss, New York, N. Y., chairman; Dr. Milton J. Matzner, Brooklyn, N. Y.; Dr. Michael W. Shutkin, Milwaukee, Wisc.; Dr. James T. Nix, New Orleans, La.

Endowment Fund Committee:—Dr. William C. Jacobson, New York, N. Y., chairman; Dr. William W. Lermann, Pittsburgh, Pa.; Dr. Elihu Katz, New York, N. Y.; Dr. Felix Cunha, San Francisco, Calif.

Research Committee:—Dr. H. Necheles, Chicago, Ill., chairman; Dr. Samuel Berger, Cleveland, Ohio; Dr. Bernard J. Ficarra, Brooklyn, N. Y.; Dr. Elihu Katz, New York, N. Y.; Dr. George B. Jerzy Glass, New York, N. Y.

Convention Committee:—Dr. William C. Jacobson, New York, N. Y.; Dr. Joseph Shaiken, Milwaukee, Wisc.; Dr. Elihu Katz, New York, N. Y.; Dr. Samuel Weiss, New York, N. Y.

Postgraduate Education Committee:—Dr. William W. Lermann, Pittsburgh, Pa., chairman; Dr. Karver L. Puestow, Milwaukee, Wisc.; Dr. Louis H. Clerf, Philadelphia, Pa.; Dr. Joseph Shaiken, Milwaukee, Wisc.; Dr. C. Wilmer Wirts, Philadelphia, Pa.; Dr. Roy Upham, New York, N. Y.; Dr. John W. Means, Columbus, Ohio; ex-officio, Dr. Owen H. Wangensteen, Minneapolis, Minn.; Dr. I. Snapper, Brooklyn, N. Y.

Nominating Committee:—Dr. Sigurd W. Johnsen, Passaic, N. J., chairman; Dr. Lynn A. Ferguson, Grand Rapids, Mich.; Dr. William E. Bippus, Miami Beach, Fla.; Dr. Harry Barowsky, New York, N. Y.; Dr. Michael W. Shutkin, Milwaukee, Wisc.

Other committees appointed were:

Constitutional Revision Committee:—Dr. Sigurd W. Johnsen, Passaic, N. J., chairman; Dr. Lynn A. Ferguson, Grand Rapids, Mich.; Dr. James T. Nix, New Orleans, La.; Dr. Arthur A. Kirchner, Los Angeles, Calif.; Dr. C. Wilmer Wirts, Philadelphia, Pa.; Dr. Frank J. Borrelli, New York, N. Y.; ex-officio, Dr. Anthony Bassler, New York, N. Y.; Dr. Roy Upham, New York, N. Y.

Public Relations Committee:—Dr. John E. Cox, Memphis, Tenn., chairman; Dr. Lynn A. Ferguson, Grand Rapids, Mich.; Dr. William B. Rawls, New York, N. Y.; Dr. Robert B. Hope, Los Angeles, Calif.

Exploratory Committee:—Dr. C. J. Tidmarsh, Montreal, Canada, chairman; Dr. William W. Lermann, Pittsburgh, Pa.; Dr. Frank J. Borrelli, New York, N. Y.; ex-officio, Dr. Anthony Bassler, New York, N. Y.; Dr. Sigurd W. Johnsen, Passaic, N. J.

The Council approved a President's message page to be carried in each issue of THE REVIEW OF GASTROENTEROLOGY.

The Secretary, Dr. A. Xerxes Rossien, reported that the changes in the constitution and by-laws which were adopted on Monday left a vacancy on the Council and under the provisions of the constitution and by-laws, the Council then unanimously elected Dr. M. E. Steinberg of Portland, Oregon, to fill the vacancy.

Dr. Johnsen requested that the change to regions be implemented by appointing regional representatives.

Upon motion duly made, seconded and carried, the following were appointed regional representatives for the coming year. Eastern region, Dr. I. R. Jankelson, Boston, Mass.; Southern region, Dr. John E. Cox, Memphis, Tenn.; Western region, Dr. Donald C. Collins, Los Angeles, Calif.; Central region, Dr. Joseph Shaiken, Milwaukee, Wisc. and Foreign region, Dr. Fernando Milanes, Havana, Cuba.

Dr. Roy Upham, Secretary-General, presented for consideration the first regional meeting to be held in Milwaukee, Wisc. at a date and time suitable to

the local representatives. Dr. Joseph Shaiken of Milwaukee was appointed to arrange for the regional meeting.

Upon motion duly made, seconded and carried, the following resolution was adopted:

"It is hereby resolved that steps be taken to activate the American College of Gastroenterology as promptly as possible."

Dr. Johnsen reported that a charter had been granted to the American College of Gastroenterology in Delaware in 1952 and that by resolution, the officers of the National Gastroenterological Association were to serve as the officers of the American College of Gastroenterology.

A motion duly made, seconded and carried authorized the change of name of the official publication of the National Gastroenterological Association from The Review of Gastroenterology to that of THE AMERICAN JOURNAL OF GASTROENTEROLOGY effective 1 January 1954.

ELECTION OF OFFICERS

At the Annual Meeting of the National Gastroenterological Association held in Los Angeles, Calif., on 12 October 1953, the following officers were elected for 1953-1954: President-elect, Dr. Lynn A. Ferguson, Grand Rapids, Mich.; 1st Vice-President, Dr. James T. Nix, New Orleans, La.; 2nd Vice-President, Dr. Arthur A. Kirchner, Los Angeles, Calif.; 3rd Vice-President, Dr. C. Wilmer Wirts, Philadelphia, Pa.; 4th Vice-President, Dr. Frank J. Borrelli, New York, N. Y.; Secretary-General, Dr. Roy Upham, New York, N. Y.; Secretary, Dr. A. Xerxes Rossien, Kew Gardens, N. Y. and Treasurer, Dr. Elihu Katz, New York, N. Y.

Members of the National Council elected for 4 years are: Dr. Yves Chaput, Montreal, Canada; Dr. John E. Cox, Memphis, Tenn.; Dr. I. R. Jankelson, Boston, Mass.; Dr. Fernando Milanes, Havana, Cuba; Dr. S. Bernard Kaplan, Newark, N. J.

Dr. William B. Rawls of New York City was elected to fill the vacancy of the unexpired term on the Council of Dr. Frank J. Borrelli, who was elected 4th Vice-President of the Association.

ERRATA

Through an error, the program for the Course in Postgraduate Gastroenterology of the National Gastroenterological Association omitted the names of the co-authors of one of the papers presented.

Paper number 19 listed on page XVIII of the program should have appeared as follows.

19.

"Amebiasis in Tuberculosis Patients".

Speakers.

Dr. A. Xerxes Rossien, Kew Gardens, N. Y.; Dr. K. G. Dwork, Forest Hills, N. Y. and Deborah Friedman, M. S., New York, N. Y.

We sincerely regret this error of omission and the names of the co-authors appear with the article published in this issue.

In Memoriam

We record with profound sorrow the passing of our Honorary Fellow and first President, Dr. G. Randolph Manning of New York City.

Dr. Manning, following his term of office as President of the Association, served as the Secretary for many years until his election as an Honorary Fellow of the Association in 1949.

The National Gastroenterological Association has experienced a great loss in the passing of Dr. Manning and we extend our deepest sympathies to Mrs. Manning.

ABSTRACTS FOR GASTROENTEROLOGISTS

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LIVER AND BILIARY TRACT

EFFECT OF THERAPEUTIC IRRADIATION OF CARCINOMA OF CERVIX ON LIVER FUNCTION: J. R. Snevely, R. H. Bullington and J. V. Schlosser. A.M.A. Arch. Int. Med., 92:195-203, 1953.

Serial liver function tests were performed on 15 patients with carcinoma of the cervix treated by a combination of x-ray and radium irradiation. A significant retention of sulfabromophthalein was observed in the majority of cases. This transient disturbance is probably a response of the liver to the stress of irradiation or to specific chemical substances produced by ionizing radiation of tissues or by tissue necrosis. A decrease of the concentration of total serum lipids, abnormal zinc turbidity and cephalin flocculation tests develop only in scattered cases, while thymol tyrbidity, thymol flocculation and total serum bilirubin showed no significant alterations.

H. B. EISENSTADT

RESIDUALS OF YELLOW FEVER VACCINE AFTER TEN YEARS—A MEDICAL AND LEGAL PROBLEM: Irving B. Brick. A.M.A. Arch. Int. Med., 92:221-227, 1953.

An epidemic of jaundice followed innoculations of Yellow Fever Vaccine in personnel of the U. S. Armed Forces in 1942. The cases of 15 patients who received this vaccine and suffered from chronic liver disease several years later are reported. Only 7 of them had recognizable hepatitis or jaundice in the usual incubation period. The diagnosis of chronic hepatitis, atrophic cirrhosis or postnecrotic cirrhosis was made either by liver biopsy or autopsy in these cases. The relationship between the vaccination and the chronic liver disease was difficult to prove in those cases with the history of alcoholism as well as in others where no acute phase of jaundice or hepatitis was observed. It has been estimated on the basis of random samples that twice as many patients had hepatitis without jaundice as had hepatitis with jaundice following Yellow Fever Vaccination. It is possible that the majority of the anicteric cases were never recognized. The prognosis in regard to permanent liver damage might be worse in the latter individuals because they had never received any form of treatment. The legal implications of government compensation for death or disability are also discussed.

H. B. EISENSTADT

LIVER DYSFUNCTION IN HEPATOLENTICULAR DEGENERATION: Edward C. Franklin and Arthur Bauman. Am. J. Med. 15:450, (Oct.), 1953.

Contrary to the statement of Wilson that patients with this disease show a cirrhosis of the liver at autopsy but rarely any symptoms and signs during lifetime, clinical findings of a hepatic disorder were present in 7 persons of a group of 11. Five of these developed hepatic symptomatology prior to any nervous manifestations. Splenomegaly, ascites, jaundice, hepatomegaly, hematemesis and spider angiomas were found. Vari-

ous abnormal liver function tests were noticed in most patients as positive cephalin flocculation and thymol turbidity tests, elevated alkaline phosphatase and low prothrombin time, serum protein and serum cholesterol. Abnormal hepatic function may be found even in those cases where clinical signs and symptoms are absent but they are frequently not looked for. The main causes of death of patients with Wilson's disease are hepatic failure, massive hematemesis and intercurrent infections.

H. B. EISENSTADT

SALINE CONCENTRATION IN CHOLECYSTOGRAPHY: P. S. Friedman and L. Solis-Cohen. Am. J. Roentgenol., pp. 437-440, (Sept.), 1953.

Oral administration of saline (80 per cent Sodium Sulfate, 20 per cent Magnesium Sulfate) during cholecystography was shown by the authors to improve visualization of poorly functioning gallbladders with calculi. When faint visualization occurs, one teaspoon of the saline mixture is dissolved in 50 c.c. of water and given orally. Film studies are then made in the erect and recumbent postures, 10 minutes, 30 minutes, and 45 minutes afterwards. The authors believe that the improved visualization probably results primarily from a transitory rise in gallbladder tone and intracystic pressure in the absence of emptying with consequent increased water absorption. It may be secondarily affected by an increase in hepatic bile secretion.

J. R. VAN DYNE

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** Steigmann, F., and Goldberg, E., J. Lab. & Clin. Med. 42:955 (1953)

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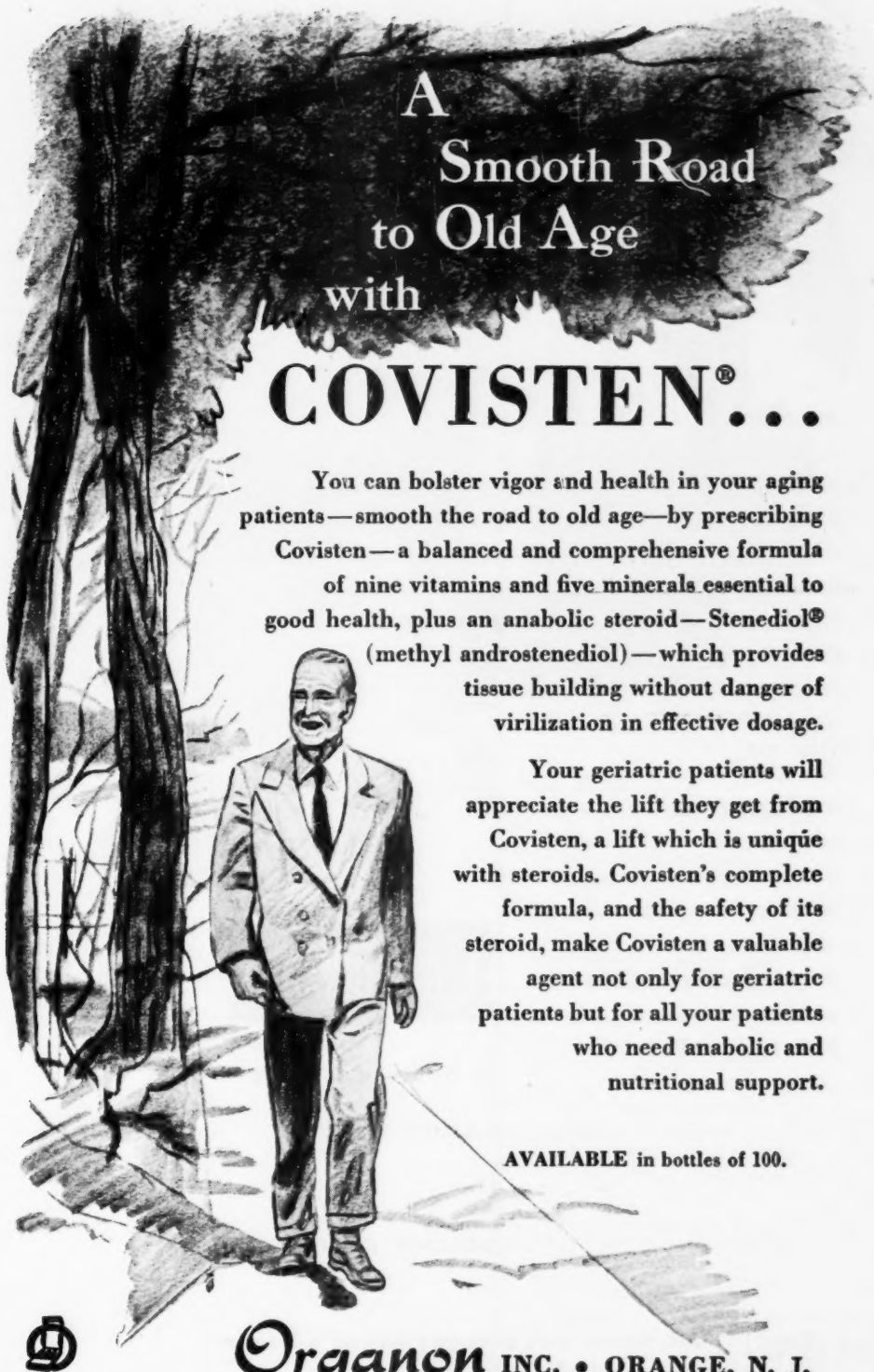

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1. Rowen, B.R., Bachrach, W.H., Halsted, J.A., and Schapiro, H.: Gastroenterology 24:86, 1953.
2. Rogers, M.P., and Gray, C.L.: Am. J. Digest. Dis. 19:180, 1952.
3. Schaub, K.: Praxis 41:1073, 1952.

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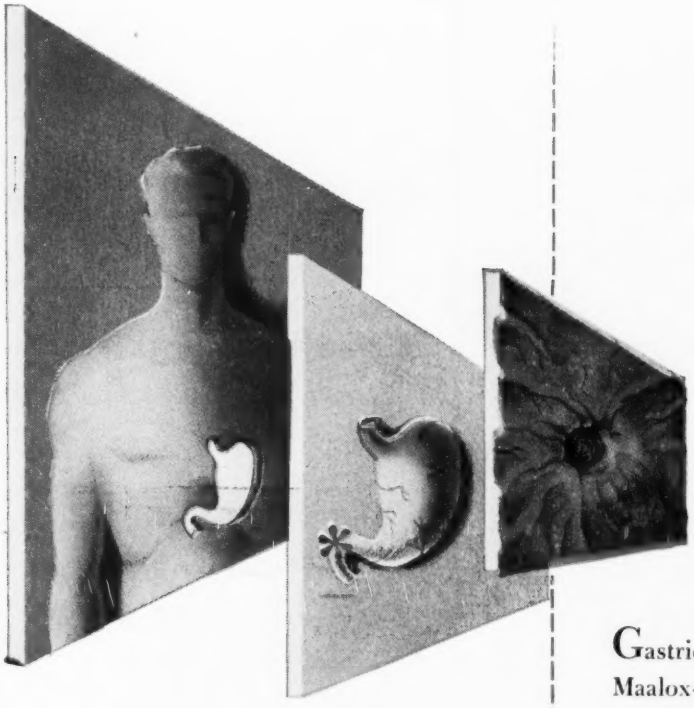

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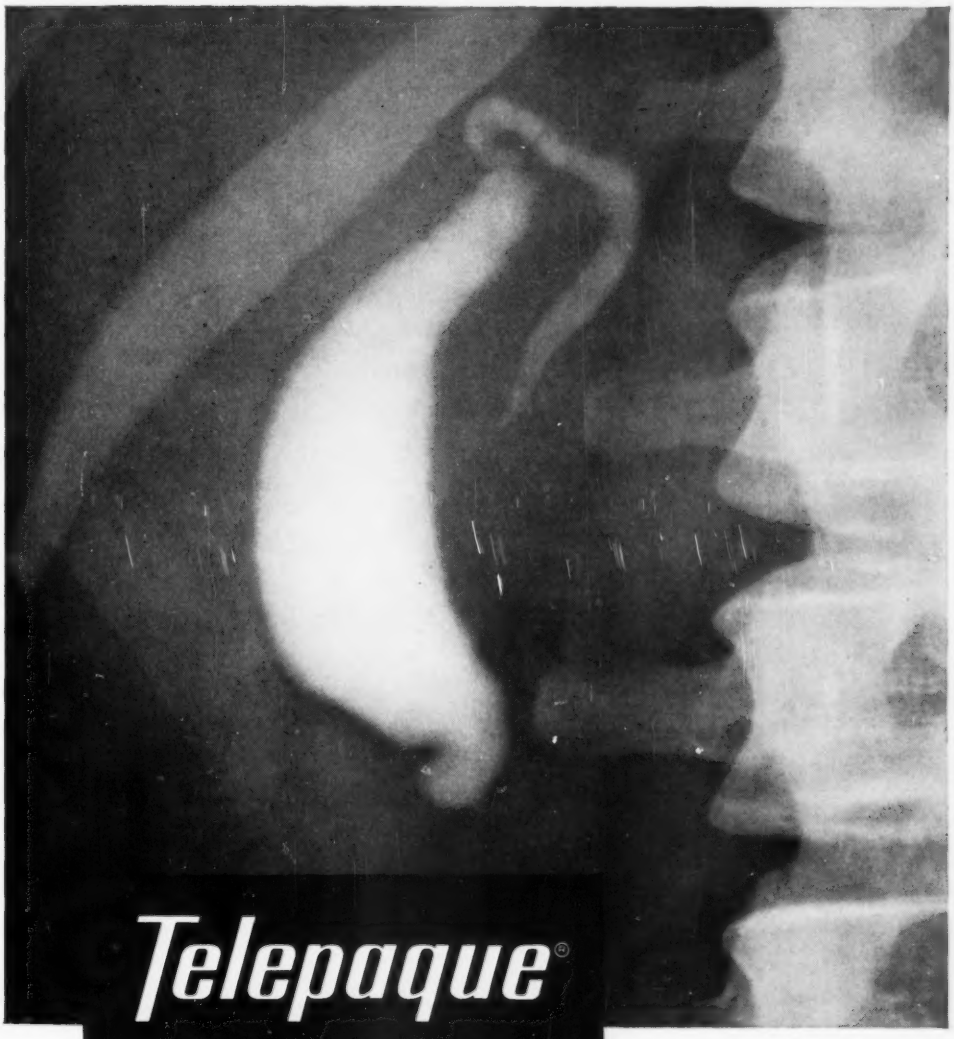

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